ACUTE CARE SURGERY ON KIDNEY TRANSPLANT RECIPIENTS: PERSPECTIVES, PRACTICES, AND OUTCOMES

by
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ABSTRACT

With improved medical and surgical care, kidney transplant recipients (KTR) are living longer than ever before. When KTR require acute care (AC) surgery for non-transplant issues, it is unclear who should manage this unique population and what specific risks KTR face during the course of surgical care.

To elucidate surgeon perspectives on acute care surgical management of transplant recipients, we designed and nationally administered a survey to transplant and AC surgeons. We then investigated the differences in mortality, morbidity, length of stay (LOS) and cost between KTR and non-transplant recipients (non-KTR) undergoing appendectomy, cholecystectomy and colorectal resection as a retrospective cohort study using data from the National Inpatient Sample and adjusting for patient and hospital level factors.

There were 230 survey participants who were AC surgeons (response rate 14%) and 204 from transplant surgeons (response rate 20%). Both AC and transplant surgeons (78% and 100%) agreed that KTR care would be better at transplant centers, and that KTR requiring urgent surgery should be transferred to a transplant center if possible (80.2% and 87.2%). However, AC surgeons with more years of practice were less likely to transfer KTR to a transplant center ($p = 0.03$). In the national cohort study of appendectomy, complications were similar among KTR and non-KTR, while LOS and costs were greater for KTR (LOS ratio $_{1.19}1.31_{1.45}$; cost ratio $_{1.11}1.17_{1.26}$). For cholecystectomy, KTR had higher mortality (2.7% vs 1.2%, $p<0.001$), morbidity (18.8% vs 13.9%, $p<0.001$; aOR 1.30 95%CI 1.12-1.51), LOS and costs (LOS ratio $_{1.17}1.23_{1.28}$ 1.23; cost ratio $_{1.08}1.13_{1.17}$1.13). For colorectal resection, KTR had higher mortality (11.1 vs 4.3%, $p <0.001$; aOR $_{2.68}3.59_{4.81}$), morbidity (38.5 vs 31.5%, $p =0.001$; aOR $_{1.08}1.30_{1.56}$), LOS and costs (LOS ratio $_{1.42}1.53_{1.65}$; cost ratio $_{1.42}1.54_{1.63}$).

Both AC and transplant surgeons recommend managing KTR at transplant centers. While KTR did not have higher mortality or morbidity following appendectomy, they had higher mortality,

morbidity, longer LOS and greater cost following cholecystectomy and colorectal resection. Surgeons should consider these elevated risks when planning for surgery for KTR and counsel patients accordingly.

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LIST OF ABBREVIATIONS

AC - acute care

ACS - acute care surgery

aOR - adjusted odds ratio

ASTS - American Society of Transplant Surgeons

CI - confidence interval

EAST - Eastern Association for the Surgery of Trauma

ICD-9 - International Classification of Diseases, 9th Revision

IRB - institutional review board

KTR - kidney transplant recipient

LOS - length of stay

TR- transplant recipient

Chapter 1. Introduction

Nearly 400,000 patients have had kidney transplants since 1988, and with innovations in immunosuppressive and medical therapy, kidney transplant recipients (KTR) are living longer than ever with their transplanted organs.[1–3] As these unique patients continue to live longer with functioning allografts, surgeons will see more KTR presenting with acute surgical conditions such as appendicitis and cholecystitis that require surgical intervention. Despite the growing number of transplant recipients and the potentially compounding effect of transplant history on acute care surgery outcomes, there is very little data to support decision making for these patients.

Appendicitis is one of the most common surgical diseases in the United States, with a lifetime risk of 6.7% in females and 8.6% in males.[4] While post-appendectomy morbidity is low (4.1-6.4%) and post-operative length of stay (LOS) is short (0-2.4 days) in the general population, the cumulative effect of previous kidney transplant and appendectomy on post-operative morbidity, LOS, and hospital-associated cost has not been characterized.[5,6] Additionally, the surgical approach for appendectomy has changed over time. Currently, laparoscopic appendectomy is the standard approach, with 76% of appendectomies performed laparoscopically as of 2010.[6] However, controversy still exists regarding the safety and appropriateness of the laparoscopic approach for transplant recipients. While a recent review advocated for the broader application of laparoscopy in KTR, it only cited a 2-patient case series of KTR safely undergoing appendectomy.[7,8] The lack of literature supporting the safety of laparoscopic appendectomy among KTR may inhibit more widespread utilization of this approach, which might otherwise provide a safer and lower-cost option for these patients.[5]

Cholecystectomy is also one of the most common general surgery procedures performed in the United States, with more than 400,000 cases performed every year.[9,10] Post-cholecystectomy

morbidity and mortality are low with an average hospital LOS of two days.[11–13] KTR, however, are at higher risk of developing gallstones and biliary disease than the general population due to their history of renal failure and immunosuppressive medications such as calcineurin inhibitors.[14,15] This additional risk combined with improved post-transplant survival has led to a higher incidence of cholecystectomy in the kidney transplant population in recent years.[16] Despite this, the potential cumulative effect of transplant history on cholecystectomy outcomes remains uncharacterized.[9,14]

Finally, more than 300,000 colectomies are performed annually in the United States for a variety of pathologies, including diverticulitis and cancer.[17,18] Transplant recipients have 2.6-fold higher incidence of colorectal cancer than non-transplant recipients[19], with a 5-year cumulative incidence rate of 0.5%.[20] Kidney transplant recipients also have a higher incidence of acute diverticulitis than the general population (0.94% vs 0.02%).[21] Because transplant recipients are at increased risk of these diseases, they are more likely to require colorectal resections as compared to the general population. Despite their increased need for acute care surgery intervention, it is unclear who should perform these non-transplant acute care surgeries and where this care should be delivered.

Surgeons continue to express concerns about increased risk of morbidity, mortality, longer LOS, and higher costs of care for transplant recipients, although not all of these concerns are necessarily evidence based. Studies of cardiac and lung transplant recipients undergoing cholecystectomy and hernia repair suggest that mortality and morbidity are not significantly elevated in this population and that transplant status should not be prohibitive of pursuing surgical treatment.[22,23] Other studies have reported that post-operative outcomes for solid organ transplant recipients following general surgical procedures are worse than the general population, with a recent review citing up to 32.7% mortality and 17.5% morbidity for emergency abdominal surgery, in comparison to 5.5% mortality and 9% morbidity in non-transplant recipients.[6,9] However, many transplant physicians feel that

morbidity, LOS and cost might be mitigated if transplant recipients receive their surgical care at transplant centers.[24,25]

The argument that transplant recipients incur longer lengths of stay and higher costs after general surgery remains controversial as well. Taghavi et al. demonstrated that solid-organ transplant recipients remained in the hospital for 4-8 days following cholecystectomy as compared to a median of one day among non-transplant recipients.[11,22] In a review, De'Angelis et al. reported a median LOS of 22.2 days following colorectal resection for kidney transplant recipients as compared to a national average of 9.3 days.[9,26] To date, no studies have investigated cost differences in surgical care for transplant recipients as compared to non-transplant recipients for non-transplant surgical intervention, and none of the studies addressing length of stay discuss outcomes by center type.[27–29]

Book chapters discussing non-transplant surgery in transplant recipients warn that complications are higher and that these medically complex patients should be treated at transplant centers to avoid undue complications.[24,30,31] These references primarily serve to guide preoperative optimization of transplant recipients and to caution general surgeons from underestimating the risks of treating this unique population. However, there is no substantial evidence that care for non-transplant related surgeries at transplant centers improves outcomes. There is limited data to support that these patients will benefit from transfer, and these studies focus on medication adherence and graft rejection, rather than on surgical outcomes directly.[3,32,33] There are currently no studies that document perspectives of acute care surgeons on the treatment of transplant recipients. Additionally, transplant surgeons, who are board certified in general surgery, have practices that span acute care surgery in transplant recipients.[34] To what degree transplant surgeons feel comfortable performing acute care surgery on transplant recipients is also unknown, yet might greatly inform practice and potential transfer of these patients.[35] A previously published survey of surgeon members of the

American Society of Transplant Surgeons collected responses from 171 transplant surgeons, and found that 80% perform general surgery cases with a median of 55 general surgery cases per year.[34] Most importantly, transplant recipients may benefit more than non-transplant patients by undergoing surgery at a transplant center, and this should be investigated.

An improved understanding of mortality, morbidity, length of stay, and associated cost of treating kidney transplant recipients at transplant centers and at non-transplant centers is critical for peri-operative planning and risk stratification within a population of unique and potentially higher-risk patients. As such, this dissertation seeks to address these research questions in order to improve decision making for physicians and their previously transplanted patients.

In Chapter 2, we used a nationally distributed focus-group-tested survey to delineate acute care surgeon and transplant surgeon perspectives and practices with respect to previous transplant recipients. We hypothesized that acute care surgeons in non-transplant centers would rather transfer transplant recipients, even for urgent surgical needs to transplant centers, believing that transplant centers provide better care and superior outcomes in terms of length of stay and cost. We hypothesized that acute care surgeons with more experience (higher case volume and more years in practice) would feel more comfortable operating on transplant recipients and would be less inclined to transfer them to transplant surgeons for surgery. Additionally, we hypothesized that transplant surgeons would desire to perform acute care surgery on transplant recipients themselves, and would support transfer of these unique patients to transplant centers.

In Chapters 3-5, we investigated differences in mortality, morbidity, length of stay, and cost between kidney transplant recipients and non-transplant patients undergoing acute care surgical procedures.

We hypothesized that kidney transplant recipients would have higher mortality and morbidity than non-transplant recipients following acute care surgery. We anticipated a longer LOS and a higher cost for kidney transplant recipients. We hypothesized that outcomes for kidney transplant centers would vary by the center type. Specifically, we expected that among kidney transplant recipients, those who had acute care surgery at transplant centers would have better outcomes than at non-transplant centers. To investigate these outcomes, we studied a large population of patients undergoing appendectomy, cholecystectomy, and colectomy using the National Inpatient Sample. In order to document differences in outcomes for kidney transplant recipients treated at transplant centers compared to those treated at non-transplant centers, we evaluated for effect measure modification by transplant center status.

Chapter 2. Acute Care Surgery for Transplant Recipients: A Cross-sectional Survey of Surgeon Perspectives and Practices

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ABSTRACT

Background. There are a growing number of transplant recipients, who with innovations in medical and surgical therapy, are living longer than ever before. When these recipients require acute care surgery for non-transplant related issues, it is unclear who should operate on and manage this unique population. We hypothesized that while both acute care and transplant surgeons would feel comfortable operating on this unique patient population, both would believe transplant centers provide superior care.

Methods. To characterize surgeon perspectives on the management of transplant recipients for non-transplant related issues, we conducted a national survey of transplant surgeons and acute care surgeons. The survey instrument was based on interviews with key informants practicing at transplant and non-transplant centers and was distributed by email. Surgeon and center specific demographics were collected; acute care and transplant surgeon preferences were compared using χ^2 tests and multivariable logistic regression.

Results. We obtained 230 responses from acute care (AC) surgeons and 204 from transplant surgeons (response rates 14% and 20%, respectively). AC surgeons and transplant surgeons agreed that care would be better at transplant centers (78% and 100%), and that transplant recipients requiring AC surgery should be transferred to a transplant center if possible (80.2% and 87.2%). AC surgeons felt comfortable operating (97.5%) and performing laparoscopic procedures (94.0%) on transplant recipients. AC surgeons with more years of practice were less likely to transfer urgent cases to a transplant center than those with fewer years ($p = 0.03$). AC surgeons cited transplant medication use (steroid or other) as the most important underlying cause of increased surgical complications for transplant recipients. Transplant surgeons felt it was their responsibility to perform AC surgery on transplant recipients (67.3%), but less so if patient underwent transplant at a different institution (26.5%). Transplant surgeons were less likely to transfer patients to an AC surgeon for an elective case (aOR 0.14 95%CI 0.05-0.40) or urgent case (aOR 0.23 95%CI 0.13-0.60) if they took

general surgery call. Transplant surgeons cited poor transplanted organ resiliency as the most important underlying cause of increased surgical complications for transplant recipients.

Conclusions. AC surgeons and transplant surgeons feel comfortable performing laparoscopic or open acute care surgery on transplant recipients, and recommend treating transplant recipients at transplant centers despite the lack of evidence to support this. Elucidating these common goals and recommendations allows surgeons to provide optimal care for this unique patient population.

BACKGROUND

Nearly 400,000 patients have had kidney transplants since 1988, and with innovations in immunosuppressive and medical therapy, they are living longer than ever with their transplanted organs.[1–3] As in the general population, these unique patients are at risk of acute surgical conditions, such as appendicitis, and will require surgical treatment. Kidney transplant recipients are at an increased risk of developing gallstones, diverticulitis, and colorectal cancer, which could all result in an increased need for acute care surgical intervention compared to the general population.[14,20,21] Despite this need, it is unclear who should perform these non-transplant acute care surgeries and where this care should be delivered.

Anecdotal evidence suggests that community surgeons feel compelled to transfer transplant recipients to transplant centers for their care. Book chapters discussing non-transplant surgery in transplant recipients warn that complications are higher and that these patients should be treated at transplant centers to avoid undue complications.[24,30,31] There is limited data to support that these patients will benefit from transfer, and the available studies focus on medication adherence and graft rejection, rather than surgical outcomes.[3,32,33] However, there are currently no studies that document perspectives of acute care surgeons on the treatment of transplant recipients. Additionally, transplant surgeons, who are board certified in general surgery, have practices that span acute care surgery in transplant recipients.[34] To what degree transplant surgeons feel comfortable performing acute care surgery on transplant recipients is also unknown.

To investigate these issues, we designed and distributed a survey to acute care and transplant surgeons nationally. We queried their individual perspectives and practice patterns for transplant recipients, and compared responses from acute care surgeons practicing at non-transplant centers, acute care surgeons practicing at transplant centers, and transplant surgeons.

METHODS

Study design and population

We conducted a cross-sectional survey of acute care (AC) and transplant surgeons regarding their perceptions and practices when treating transplant recipients who require acute care surgery intervention. We performed a pilot survey of acute care and transplant surgeons at our institution prior to distributing the survey nationally to transplant and acute care surgeons. Transplant surgeon members of the American Society of Transplant Surgeons (ASTS) comprised the transplant surgeon study population. Acute care surgeon members of the Eastern Association for the Surgery of Trauma (EAST) comprised the acute care surgeon population.

Survey development and content

The survey tool was developed following key informant interviews with two acute care surgeons from transplant centers (11/15/2016 and 11/16/2016), one acute care surgeon from a non-transplant center (11/18/2016) and one transplant surgeon (12/6/2016). The questionnaire was drafted using the domains identified in the interviews. Key informants then reviewed the questionnaire to check for clinical accuracy and applicability. We used the Qualtrics survey interface to design and administer the survey tool.

The survey instrument was divided into three sections: demographic information (6 items), individual practice information (ranging between 5 and 8 items), and "reasonable standard of care" information (between 20 and 25 items). Individual items were designed for and targeted towards one of three specific participant groups: acute care surgeons at non-transplant centers, acute care surgeons at transplant centers, and transplant surgeons. Question types varied from multiple choice to binary

yes/no, with one free text question. The final section of the survey contained five scenarios regarding transplant recipients presenting to non-transplant centers, and surgeons were asked to rank scenarios on a 1-5 Likert scale, ranging from 1 "definitely treat at non-transplant center" to 3 "transfer if possible to a transplant center" to 5 "definitely transfer to a transplant center". The questions posed to respondents varied based on their responses to demographic and individual practice information to ensure that questions were pertinent to their respective participant group. For example, a question regarding a respondent's distance away from the nearest transplant center only pertained to acute care surgeons practicing at non-transplant centers, and the Qualtrics interface allowed us to target this question towards that subpopulation. Please see Appendix A for the full questionnaire. This anonymous survey was considered exempt and acknowledged by the Johns Hopkins Hospital IRB (IRB00127443, 2/24/2017).

Pilot administration

Prior to national dissemination, we distributed the pilot questionnaire to surgical faculty at Johns Hopkins Hospital via the faculty list serve, which included general surgeons practicing at both non-transplant centers and transplant centers, as well as transplant surgeons, on 6/22/2017, with two reminder emails sent at weekly intervals. A total of 137 surgeons received a link to the survey, and 30 responses were collected (22%). Three surveys were blank or contained only demographic data, and were excluded. A total of 27 surveys were available for analysis (20%), of which 15 were completed by surgeons who did not take acute care surgery call or who were not transplant surgeons. In the pilot interface, only surgeons who responded "yes" to taking general surgery call or those who were transplant surgeons were eligible to complete the whole survey. This narrowed our pilot analysis to 12 responses (9%). Following feedback from survey respondents and department faculty, the final, nationally disseminated questionnaire allowed any respondent to complete the entire questionnaire,

whether or not they took general surgery call, allowing for further comparisons between surgeon and center subgroups.

Study population

Transplant surgeon members of the American Society of Transplant Surgery (ASTS) comprised the transplant surgeon study population. We accessed an online registry of ASTS members and cross referenced each entry using searches to exclude non-surgeon transplant providers, resulting in a list of 984 transplant surgeons. Acute care surgeon members of the Eastern Association for the Surgery of Trauma (EAST) comprised the acute care surgeon population. Permission to distribute the survey tool via the EAST membership list of trauma and acute care surgeons was sought through a formal application process. The survey was reviewed by the EAST Research-Scholarship committee and approved for distribution. The list of 1671 active, provisional, and senior members was obtained. In total, 984 transplant surgeons and 1671 acute care surgeons fulfilled criteria for study inclusion at the respective dates of distribution.

Survey administration

An IRB approved email describing the study was sent to all eligible participants. Respondents participated via an email link, and anonymous responses were collected. Beginning on 09/05/2017, ASTS members were emailed weekly up to five times, and those who elected to participate were not included in subsequent reminder mailings. Beginning on 10/05/2017, EAST members were emailed every other week up to three times, as specified by EAST survey administration guidelines. The total time from the first survey emailing to the end of the study period, including reminders, was 8 weeks.

Analytical methods

We used χ^2, Fisher's exact, and Kruskal-Wallis tests to analyze categorical and continuous variables where appropriate. Years in practice and case volume were collected and analyzed as ordinal

variables. In the logistic regression models, covariable selection was performed based on clinical relevance; model parsimony was investigated using Akaike Information Criterion. Free text answers were evaluated for themes and categorized into thematic groups by two independent analysts. For all analyses, a two-tailed p-value of < 0.05 was considered statistically significant. Confidence intervals are reported as per the method of Louis and Zeger.[36] Statistical analysis was performed using Stata 14.0 (StataCorp, College Station, Texas).

RESULTS

Study Population

Of those who received survey invitations, 204 transplant surgeons (21%) and 236 AC surgeons (14%) of whom 94 were from non-transplant centers and 136 were from transplant centers. Table 1 describes practice patterns of respondents across the three surgeon types. There was a relatively even distribution across years in practice, with 20-30% of respondents in each category except those "still in training". Case volume was lower for transplant surgeons (73% reported fewer than 200 cases per year) compared to AC surgeons (49.3% at transplant centers and 52.2% at non-transplant centers reported fewer than 200 cases per year, $p<0.001$). AC surgeons at non-transplant centers had the highest case volume (22% reporting more than 300 cases per year) and were more likely to practice in community settings (59.5%, $p <0.001$) and in rural areas (11.7%, $p<0.001$). The majority of transplant surgeons and AC surgeons at transplant centers reported practicing at academic/teaching hospitals (82.4% and 93.4% respectively) and in urban settings (84.2% and 86%). Only 11.7% of transplant surgeons reported taking general surgery call, compared to 84.4% and 97.8% of AC surgeons at transplant and non-transplant centers, respectively.

Practice Specific Responses

Transplant surgeons reported their most advanced AC surgery case type was appendectomy or cholecystectomy (basic) 27.3% of the time; in contrast, only 1.1% of AC surgeons at transplant centers and 0% at non-transplant centers listed appendectomy and cholecystectomy as their most advanced ACS case type. Among transplant surgeons 44.2% reported being comfortable performing gastrectomy or colectomy (advanced) AC surgery cases. AC surgeons reported their most advanced surgery case type was colectomy or gastrectomy (advanced) 87.3% and 80.7% of the time at transplant and non-transplant centers respectively. 76.5% of transplant surgeons reported feeling comfortable with laparoscopy compared to >95% of AC surgeons ($p < 0.001$, Table 1.)

The vast majority of all respondents reported performing acute care surgery on transplant recipients in their practice (93.5-97.5%, Table 2). AC surgeons reported performed laparoscopy on transplant recipients with more frequency than transplant surgeons (87% at non-transplant centers, 94% at transplant centers vs 77% of transplant surgeons, $p<0.001$).

Surgeon Perspectives at Transplant Centers

Surgeons at transplant centers (transplant surgeons and AC surgeons) responded "yes" more frequently to "Do transplant recipients (TR) get better care following general surgery procedures if they are cared for at transplant centers?" (95.9%, 89.7%) than AC surgeons at non-transplant centers (71.7%, $p<0.001$). Surgeons at transplant centers also felt more strongly that "Transplant recipients should be transferred to transplant centers for urgent/emergent general surgery needs whenever possible." (87.2%, 80.2% vs 57.6%, $p<0.001$, Table 2).

Sixty-seven percent of transplant surgeon respondents believed it was their responsibility to perform AC surgery on TR, whereas 77.4% of AC surgeons believed it was an AC surgeon's responsibility (p

<0.001, Table 3a). When asked about transferring a TR to the AC surgery team, 68% of transplant surgeons responded they would transfer to AC surgeons for elective cases, and 31% would transfer to AC surgeons for urgent/emergent cases (Table 3b). Among transplant surgeons who would not transfer to an AC surgeon for urgent/emergent surgery, 65.4% reported they would rarely or never request intraoperative help from AC surgeons. When asked about transferring a TR to the transplant surgery team, 35% of AC surgeons responded they would transfer to a transplant surgeon for elective surgery, and 26% would transfer to transplant surgeons for urgent/emergent surgery. The majority of AC surgeons reported they would request intraoperative assistance from a transplant surgeon in elective cases (16% would *always*, 15% *most of the time* and 27% *sometimes*, total of **58%**), and for urgent/emergent cases (17% would *always*, 26% *most of the time* and 19% *sometimes*, total of **62%**, Table 3b).

In a multivariable model, AC surgeons were more likely to report transferring elective cases to transplant surgeons if they had higher case volume (aOR $_{0.31}0.49_{0.79}$), after adjustment for years in practice, hospital setting, and hospital type (Table 5). AC surgeons were less likely to transfer urgent cases to transplant surgeons if they had more years in practice (aOR $_{0.44}0.65_{0.95}$). Transplant surgeons were less likely to transfer elective cases to AC surgeons if they had higher case volume (aOR $_{0.43}0.62_{0.91}$) or if they take general surgery call (aOR $_{0.05}0.14_{0.40}$), adjusting for years in practice and comfort with laparoscopy on TR. Transplant surgeons were less likely to transfer urgent cases to AC surgeons if they reported comfort performing laparoscopy on TR (aOR $_{0.13}0.28_{0.60}$) or if they take general surgery call (aOR $_{0.05}0.23_{1.06}$), although the latter was only marginally significant.

Perspectives of surgeons practicing at non-transplant centers

AC surgeons practicing at non-transplant centers felt they could easily (78%) or with some difficulty (22%) contact a transplant center or transplant surgeon for help with a transplant recipient. Among

AC surgeons at non-transplant centers, 41% practiced within 10 miles of a transplant center, but 33% practiced >50 miles from the nearest transplant center (Table 4). When asked about transferring TR to transplant centers, 61% would do so for elective operations and 35% would do so for urgent/emergent operations (Table 4.) Distance from transplant center was not associated with tendency to transfer TR ($p=0.4$).

Who should be transferred?

There was a linear trend in willingness to transfer TR, such that the longer time post-transplant the less likely the surgeon would transfer the TR to a transplant center. Surgeons reported the lowest need to transfer TR who were over five years out from transplantation (Figure). Surgeons reported the highest potential need to transfer TR with acute liver failure (Figure). Despite the linear relationship reported by each group, the three surgeon groups differed significantly for each scenario, such that transplant surgeons felt more strongly that each patient type should be transferred to transplant team or center ($p<0.001$, Table 6).

AC surgeons provided 99 free-text responses when asked what the number one reason would be to transfer a TR requiring acute care surgery to a transplant team or transplant center. The five most prominent themes were safety of the transplanted organ/graft, continuity of care between transplant patient and transplant team, management of perioperative medications, medical liability, and patient preference.

Transplant center expectations

Very few surgeons reported having hospital policies indicating who should perform acute care surgery on transplant recipients (16.8% of transplant surgeons, 8.6% AC surgeons at transplant

centers, and 0% of AC surgeons at non-transplant centers). When asked about cost of care for TR following acute care surgery, responses were similar across all surgeon types, with a large proportion believing the cost would be the same at transplant and non-transplant centers (p=0.3, Table 2). Regarding length of stay (LOS), surgeons felt that LOS would be longer at non-transplant centers or the same regardless of center type (p=0.2, Table 2).

Surgeon concerns

Responses were varied between surgeons on what they considered the most concerning feature of performing AC surgery on TR (p <0.001, Table 7). Transplant surgeons reported that management of postoperative medications (38.5%), higher risk of other complications (19.3%) and anatomical differences (17.2%) were the most concerning. AC surgeons at transplant centers reported that management of postoperative medications (45.9%), higher risk of other complications (22.5%) and wound healing complications (18.0%) were the most concerning. AC surgeons at non-transplant centers reported that management of postoperative medications (58.4%) and the risk of renal failure (14.6%) were the most concerning.

AC surgeons reported that non-steroid transplant medication use was the most important cause of increased complications (41.8% and 39.3% at transplant and non-transplant centers, respectively) with steroid use a close second (34.8% and 39.1%). Transplant surgeons most frequently reported that "transplanted organs being 'less resilient to insult' " was the most important cause of increased complications in transplant recipients (35.8%), and non-steroid transplant medication use was the second most common cause reported (34.2%).

DISCUSSION

We performed a national survey of transplant and acute care surgeons to elicit perspectives and practice patterns of surgeons across the United States and characterize transplant recipient management. We found that 67% of transplant surgeons felt responsible for acute care surgery in transplant recipients and 69% would perform the operation themselves if urgent or emergent. However, transplant surgeons also reported feeling less comfortable than acute care surgeons performing laparoscopic surgery on transplant recipients (77% vs 94%, $p<0.001$) and relatively few (12%) routinely take general surgery call. Additionally, transplant surgeons felt much less strongly that that they should operate on transplant recipients who received their transplant elsewhere, with only 27% indicating that transplant surgeons should operate on this group. These findings, taken together, suggest that although transplant surgeons are willing to provide acute care surgery for transplant recipients, it may be more appropriate for AC surgeons to perform these cases, particularly if laparoscopy is indicated or if the patient and transplant surgeon do not have a pre-existing relationship.

A previously published survey of surgeon members of the American Society of Transplant Surgeons collected responses from 171 transplant surgeons, and found that 80% perform general surgery cases with a median of 55 cases per year.[34] This is a slightly higher percentage than we found, particularly given that we found only 31% of transplant surgeons in our study reported performing elective general surgery cases on transplant recipients. It is important, however, to distinguish that transplant surgeons might be performing general surgery on non-transplant recipients.

In contrast to transplant surgeons, fewer AC surgeons would transfer transplant recipients needing urgent/emergent surgery (26%), but more than half would ask for help from transplant surgeons. As we found, AC surgeons report higher case volumes (48% with 200+ cases per year) than transplant surgeons (27%), and AC surgeons with higher case volumes and more years in practice were less

likely to transfer patients to transplant teams for elective and urgent cases, respectively. Recent studies have demonstrated improved outcomes of patients when treated by high volume surgeons for emergency general surgery, suggesting that surgeon experience and familiarity with the procedures and setting contribute to good outcomes.[37,38]

The vast majority of both acute care surgeons at transplant centers (89.7%) and transplant surgeons (95.9%) agreed that transplant recipients get better care at transplant centers. Prior to the performance of this survey, this sentiment was documented only anecdotally in book chapters.[24,30,31] These chapters primarily served to guide preoperative optimization of transplant recipients and to caution general surgeons from underestimating the risks of treating this unique populations. There are studies that demonstrate the benefits of pursuing future care at transplant centers, most importantly to maintain optimal transplant medication compliance.[32,33] Accordingly, this study found that the primary concern for 58.4% of AC surgeons at non-transplant centers is management of postoperative medications.

However, there is no substantial evidence that care at transplant centers for prior transplant recipients with non-transplant related surgical issues improves outcomes. Despite our findings that nearly all of the respondents surveyed would recommend transfer of transplant recipients who are <5 years out from their transplant date to a transplant center for management of an acute care surgery issue, there is no data to support that these patients will benefit from transfer. In a recent study of emergency general surgery outcomes at teaching vs non-teaching hospitals, Zafar et al found that there was no clinical difference in mortality or morbidity between patients treated at the different hospital types.[39] Although teaching hospital status is not a perfect surrogate for transplant center, 82% of transplant surgeon respondents in our study reported working at a teaching hospital, and the findings of the Zafar et al study may be generalizable to patients at transplant centers. Most

importantly, transplant recipients might benefit more than non-transplant patients from undergoing surgery at a transplant center, and this should be investigated.

The majority of all surgeons surveyed believed that hospital cost would be the same for care regardless of transplant center status. Surgeons who work at transplant centers believed the length of stay would be shorter at transplant centers, and AC surgeons at non-transplant centers believed it would be the same regardless of center type. Some literature suggests that transplant recipients will have longer lengths of stay and higher cost following certain surgical procedures, but none of the studies delineate these outcomes by center type.[27–29] Documentation of these surgical perceptions motivates future study of the potential benefits of treating transplant recipients at transplant centers.

Our study has limitations that merit discussion. Physician surveys are notorious for low response rates, and our overall response rate of 16% is lower than would be ideal.[40–43] However, our response rate is similar to other prominent studies of the surgical workforce, and has a slightly larger number of transplant surgeon respondents than a recent survey of the transplant workforce completed by the American Society of Transplant Surgeons (n=171 vs 204).[44–47] Although the potential for nonresponse bias limits the strengths of our conclusions, it has been demonstrated that higher response rate does not prevent significant nonresponse bias.[43] This study is also subject to recall bias. Acute care surgeons may be more likely to remember operating on transplant recipients if they had negative outcomes or difficulties with management. Additionally, selection of the sample population, two groups of surgeon members of professional societies, limits generalizability of findings to surgeons who would not self-select into these societies. Despite these limitations, this study is unique in its documentation of surgeon perspectives on treatment of transplant recipients requiring acute care surgery and attempts to fill knowledge gaps previously occupied by conjecture.

In conclusion, in our national survey of acute care and transplant surgeons, we found that both acute care and transplant surgeons feel comfortable performing laparoscopic or open acute care surgery on transplant recipients, and both recommend treating transplant recipients at transplant centers. Elucidating the commonalities and differences in opinions, practice patterns, and recommendations encourages the pursuit of confirmatory research to demonstrate clinical differences between transplant and non-transplant patients following acute care surgery and to demonstrate potential benefits of treatment at transplant centers. These findings will ultimately allow surgeons to make informed decisions and provide optimal care for this unique patient population.

Table 1. Demographic information of survey respondents, acute care (AC) surgeons at non-transplant centers, AC surgeons at transplant centers and transplant surgeons.

	AC Surgeon non-transplant center n (%)	**AC Surgeon transplant center n (%)**	**Transplant Surgeon n (%)**	**p value**
n	94	136	204	
Years in Practice				0.02
Still in training	0 (0.0)	6 (4.4)	24 (11.8)	
<5	24 (25.5)	33 (24.3)	43 (21.1)	
5-10	20 (21.3)	31 (22.8)	33 (16.2)	
11-20	24 (25.5)	35 (25.7)	54 (26.5)	
21+	26 (27.7)	31 (22.8)	50 (24.5)	
Case Volume				<0.001
<100	15 (16.0)	16 (11.8)	55 (27.0)	
100-200	34 (36.2)	51 (37.5)	94 (46.1)	
201-300	24 (25.5)	46 (33.8)	36 (17.6)	
300+	21 (22.3)	23 (16.9)	19 (9.3)	
Hospital Type				<0.001
Academic/Teaching	36 (38.3)	127 (93.4)	168 (82.4)	
Community w Academic Affiliation	38 (40.4)	8 (5.9)	26 (12.7)	
Community	18 (19.1)	1 (0.7)	10 (4.9)	
Hospital Setting				0.03
Urban	57 (60.6)	117 (86.0)	171 (84.2)	
Suburban	26 (27.7)	15 (11.0)	28 (13.8)	
Rural	11 (11.7)	4 (2.9)	4 (2.0)	
Take General Surgery Call	91 (97.8)	114 (84.4)	23 (11.7)	<0.001
Most Advanced ACS Case Type Performed				<0.001
Basic	1 (1.1)	0 (0.0)	21 (27.3)	
Intermediate	16 (18.2)	14 (12.7)	22 (28.6)	
Advanced	71 (80.7)	96 (87.3)	34 (44.2)	
Comfortable with Laparoscopy	90 (96.8)	113 (95.0)	153 (76.5)	<0.001

Table 2. Perspectives and opinions of acute care (AC) surgeons at non-transplant centers, AC surgeons at transplant centers and transplant surgeons on performing acute care (AC) surgery on transplant recipients (TR).

	AC surgeon at non-transplant center n (%)	**AC surgeon at transplant center n (%)**	**Transplant surgeons n (%)**	**p value**
n	94	136	204	
Performed acute care surgery on TR	87 (93.5)	116 (97.5)	193 (97.5)	0.2
Performed laparoscopy on TR recipients	80 (87.0)	109 (94.0)	151 (77.4)	<0.001
TR get better care at transplant centers	66 (71.7)	104 (89.7)	185 (95.9)	<0.001
TR should be transferred when possible to transplant centers	53 (57.6)	93 (80.2)	170 (87.2)	<0.001
Hospital has policy about who should perform AC surgery on TR				<0.001
Yes	0 (0.0)	10 (8.6)	33 (16.8)	
No	82 (89.1)	78 (67.2)	133 (67.9)	
Unsure	10 (10.9)	28 (24.1)	30 (15.3)	
Hospital cost is higher for TR at:				0.3
Transplant centers	20 (21.7)	39 (33.9)	49 (26.1)	
Non-transplant centers	20 (21.7)	25 (21.7)	47 (25.0)	
The same regardless of center type	52 (56.5)	51 (44.3)	92 (48.9)	
Length of Stay is longer for TR at:				0.2
Transplant centers	9 (9.8)	15 (13.0)	27 (14.4)	
Non-transplant centers	35 (38.0)	53 (46.1)	90 (47.9)	
The same regardless of center type	48 (52.2)	47 (40.9)	71 (37.8)	

Table 3a. Opinions regarding performing acute care surgery on transplant recipients (TR) from only surgeons who practice at transplant centers.

	AC surgeons at transplant center n (%)	**Transplant surgeons n (%)**	**p value**
Transplant surgeons should perform ACS on TR	26 (22.6)	132 (67.3)	<0.001
AC surgeons should perform AC surgery on TR	89 (77.4)	64 (32.7)	<0.001
Who should perform AC surgery if TR received transplant at different hospital?			<0.001
AC surgeons	83 (71.6)	54 (27.6)	
Transplant surgeons	5 (4.3)	52 (26.5)	
Either/It depends	28 (24.1)	90 (45.9)	

Table 3b. Opinions from surgeons at transplant centers regarding transferring transplant recipients to other teams (ACS vs transplant) and asking for assistance from other team (ACS vs transplant) when performing acute care surgery on transplant recipients (TR).

	n (%)
AC surgeons	136
Would refer TR to **transplant surgeon** for **elective** general surgery procedure	42 (35.2)
Would transfer TR to **transplant surgeon** for **urgent/emergent** surgery	31 (26.0)
Would ask for intraoperative help from **transplant surgeon** in **elective** surgery for TR	
Always	19 (16.0)
Most of the time	18 (15.1)
Sometimes	32 (26.9)
Rarely	38 (31.9)
Never	12 (10.0)
Would ask for intraoperative help from **transplant surgeon** in **urgent/ emergent** surgery for TR	
Always	20 (16.8)
Most of the time	31 (26.0)
Sometimes	23 (19.3)
Rarely	36 (30.25)
Never	9 (7.5)
Transplant surgeons	204
Would refer TR to **AC surgeon** for **elective** general surgery procedure	
Yes, in all cases	25 (12.5)
Yes, but only complex procedures	111 (55.5)
No	64 (32)
Would transfer TR to **AC surgeon** for **urgent/emergent** surgery	62 (31)
Would ask for intraoperative help from **AC surgeon** in **urgent/emergent** surgery for TR	
Always	0 (0.0)
Most of the time	6 (4.4)
Sometimes	41 (30.1)
Rarely	62 (45.6)
Never	27 (19.8)

Table 4. Practice details and perspectives unique to acute care (AC) surgeons at non-transplant centers.

	AC surgeons at non-transplant centers (n=94) n (%)
Distance to nearest transplant center	
<10 miles	39 (41)
10-19 miles	11 (12)
20-49 miles	13 (14)
50-100 miles	16 (17)
>100 miles	15 (16)
Do you have the ability to contact transplant center or transplant surgeon for help?	
yes, easily	72 (78)
yes, but it would be difficult	20 (22)
no	0 (0.0)
Would transfer TR needing ELECTIVE operation?	57 (61)
Would transfer TR needing URGENT/EMERGENT operation?	33 (35)

Table 5. Multivariable logistic regression models for acute care and transplant surgeons regarding transfer of transplant recipients for elective or urgent/emergent surgical needs. Years in practice and case volume treated as ordinal variables; take general surgery call and performing laparoscopy on TR were binary variables.

	OR	95% CI	p value
AC Surgeons **elective** transfer			
years in practice^	0.85	0.60 - 1.20	0.4
case volume*	**0.50**	**0.31 - 0.81**	**0.005**
hospital setting	0.85	0.30 - 2.40	0.7
rural	ref	ref	ref
suburban	0.92	0.07 - 12.56	0.9
urban	1.18	0.11 - 12.78	0.9
AC Surgeons **urgent** transfer			
years in practice^	**0.66**	**0.44 - 0.96**	**0.03**
case volume*	0.67	0.40 - 1.08	0.12
hospital setting			
rural	ref	ref	ref
suburban	0.37	0.02 - 6.09	0.5
urban	0.69	0.06 - 7.98	0.8
Transplant Surgeons **elective** transfer			
years in practice^	1.07	0.82-1.39	0.6
case volume*	**0.62**	**0.43-0.91**	**0.015**
take general surgery call	**0.14**	**0.05 - 0.40**	**<0.001**
perform laparoscopy on TR	1.04	0.46 - 2.35	0.9
Transplant Surgeons **urgent** transfer			
years in practice^	0.79	0.60-1.04	0.09
case volume*	0.86	0.58-1.27	0.4
take general surgery call	**0.23**	**0.05-1.06**	**0.06**
perform laparoscopy on TR	**0.28**	**0.13-0.60**	**0.049**

^ years in practice treated as ordinal variable: still in training, <5yrs, 5-10yrs, 11-20yrs, >21yrs
*case volume treated as ordinal variable: <100 cases/year, 100-200 cases/year, 200-300 cases/year, >300 cases per year

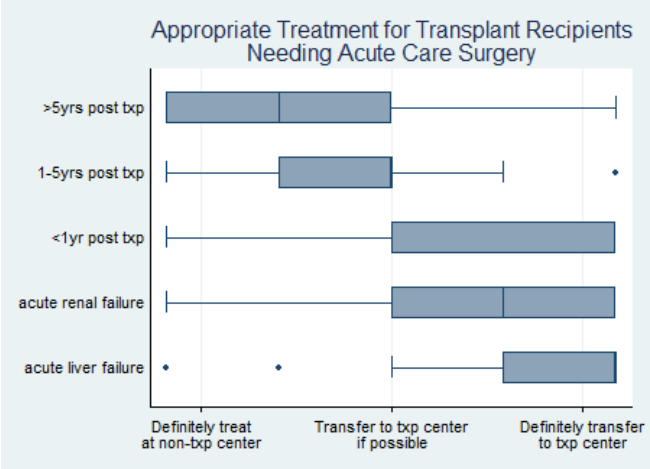
Table 6. Most concerning risks and cause of complications from the acute care (AC) and transplant surgeon perspective.

	AC surgeon at non-transplant center n (%)	**AC surgeon at transplant center n (%)**	**Transplant surgeon n (%)**	**p value**
n	94	136	204	
Most concerning about performing AC surgery on TR?				
Management of postoperative medications	52 (58.4)	51 (45.9)	74 (38.5)	
Wound healing complications	13 (14.6)	20 (18.0)	14 (7.3)	
Higher risk of other complications	9 (10.1)	25 (22.5)	37 (19.3)	
Anatomical differences	4 (4.5)	7 (6.3)	33 (17.2)	<0.001
Increased risk of mortality	3 (3.4)	2 (1.8)	15 (7.8)	
Risk of renal failure	3 (3.4)	2 (1.8)	6 (3.1)	
Other	5 (5.6)	4 (3.6)	13 (6.8)	
Most important cause of increased complications?				<0.001
Steroid use	31 (34.8)	43 (39.1)	33 (17.4)	
Other transplant medication use	35 (39.3)	46 (41.8)	65 (34.2)	
Transplanted organs less resilient to insult (acute renal failure, acute liver failure)	20 (22.5)	15 (13.6)	68 (35.8)	
History of organ failure causing irreparable damage to tissues	2 (2.2)	1 (0.9)	11 (5.8)	
Other	1 (1.1)	5 (4.5)	13 (6.8)	

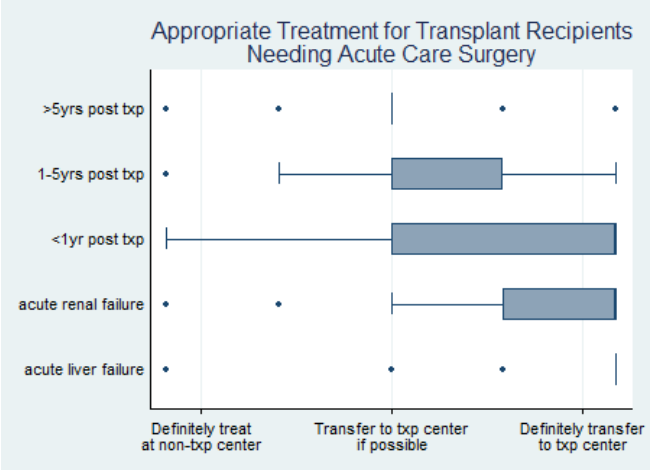
Table 7. Acute care (AC) surgeons and transplant surgeons describe what they feel the appropriate treatment would be for a transplant recipient who presents with an urgent/emergent surgery need at a non-transplant center. Scale is 1-5, with 1 "definitely treat at non-transplant center", 3 "transfer if possible to a transplant center, but not necessary" and 5 "definitely transfer to a transplant center". Values in table presented as median (IQR).

	AC surgeon at non-transplant center (n=94)	AC surgeon at transplant center (n=136)	Transplant surgeon (n=204)	p value
>5yrs from transplant	2 (1,3)	3 (2,3)	3 (3,3)	<0.001
1-5yrs from transplant	3 (2,3)	3 (3,4)	3 (3,4)	<0.001
<1yr from transplant	3 (3,5)	5 (3,5)	5 (3,5)	<0.001
Acute renal failure	4 (3,5)	5 (4,5)	5 (4,5)	<0.001
Acute liver failure	5 (4,5)	5 (5,5)	5 (5,5)	<0.001

(a)



(b)



(c)

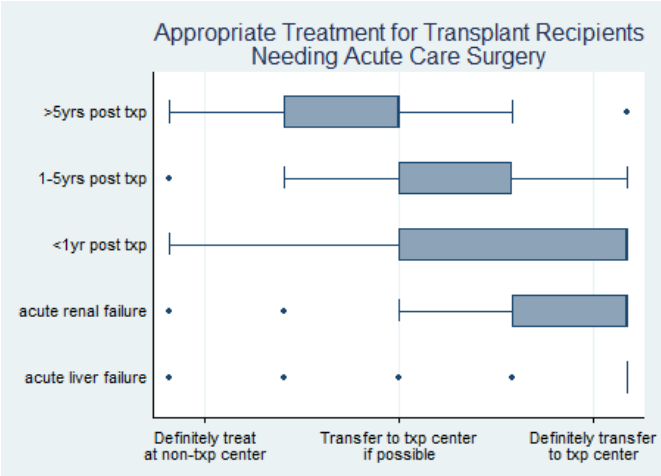


Figure. (a) Acute care surgeons at non-transplant centers (b) acute care surgeons at transplant centers and (c) transplant surgeons delineate which cases of transplant recipients requiring urgent/emergent general surgery should be transferred if presenting at a non-transplant center.

Chapter 3. Surgical Approach, Cost, and Complications of Appendectomy in Kidney Transplant Recipients

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ABSTRACT

Kidney transplant recipients (KTR) have greater morbidity and length of stay (LOS) following certain surgical procedures than non-KTR. Given that appendectomy is one of the most common surgical procedures, we investigated differences in outcomes between 1336 KTR and 2,640,247 non-KTR post-appendectomy at transplant and non-transplant centers in the US from 2000-2011, using NIS data and adjusting for patient and hospital level factors. Postoperative complications were identified using ICD9 codes. Among KTR, there were no post-appendectomy in-hospital deaths, compared to a 0.2% in non-KTR (p=0.5). Overall complications were similar among KTR and non-KTR (17.0% vs 11.6%; aOR $_{0.77}1.12_{1.61}$). LOS and costs were greater for KTR compared to non-KTR (LOS ratio $_{1.19}1.31_{1.45}$; cost ratio $_{1.11}1.17_{1.26}$). Only 44.8% of KTR had laparoscopic approach compared to 54.5% of non-KTR, but had similar complication rates (10.6 vs 8.7%, p 0.5). When treated at transplant centers, KTR had similar complications (aOR $_{0.44}0.79_{1.43}$), but longer LOS (ratio $_{1.21}1.37_{1.55}$) and greater hospital-associated costs (ratio $_{1.19}1.29_{1.41}$) than non-KTR. Conversely, at non-transplant centers, KTR and non-KTR had similar complications (aOR $_{0.75}1.23_{2.0}$), LOS (ratio $_{0.84}0.96_{1.09}$), and cost (ratio $_{0.93}1.01_{1.10}$). Contrary to results from other procedures, KTR did not constitute a high-risk group for patients undergoing appendectomy.

INTRODUCTION

Appendicitis is one of the most common surgical diseases in the United States, with a lifetime risk of 6.7% in females and 8.6% in males.[4] As in the general population, kidney transplant recipients (KTR) are at risk of requiring appendectomy, although the incidence of appendicitis in KTR has not been well documented outside of small case series.[9,48–54] Further, while post-appendectomy morbidity is low in the general population (4.1-6.4%) and average post-operative length of stay (LOS) is short (0-2.4 days), it is unknown if risk, LOS, and thus hospital associated cost is amplified for KTR.[5,6] As post-transplant survival improves, the number of KTR undergoing appendectomy will likely increase proportionally.[48,55,56] Therefore, improved understanding of morbidity, length of stay, and associated cost in this population is important for peri-operative planning and risk stratification.

Previous studies have reported that post-operative outcomes for solid organ transplant recipients following general surgical procedures are worse than the general population, with a recent review citing up to 32.7% mortality and 17.5% morbidity for emergency abdominal surgery, in comparison to 9% morbidity in non-transplant recipients.[6,9] For appendectomy specifically, in the largest case-series to date that included transplant recipients, there were only 17 appendectomies reported, and only 3 of those performed on KTR. In this small population, the documented complication rate was surprisingly high at 24%. Additionally, these patients had a mean length of stay of 7 days, compared to a median 1 day reported recently for non-transplant patients.[6,48] However, many transplant providers feel that morbidity, LOS and cost might be mitigated if transplant recipients receive their surgical care at transplant centers.[24,25]

Additionally, the surgical approach for appendectomy has changed over time. Currently, laparoscopic appendectomy is the standard approach, with 76% of appendectomies performed laparoscopically as of 2010.[6] However, controversy still exists regarding the safety and appropriateness of the

laparoscopic approach for transplant recipients. While a recent review discussing the role of laparoscopy in transplant recipients advocated for the broader application of laparoscopy in the KTR population, it only cited a 2-patient case series of KTR safely undergoing appendectomy.[7,8] The lack of literature supporting the safety of laparoscopic appendectomy among KTR may be inhibiting more widespread utilization of this approach.

To investigate the differences in surgical approach, mortality, morbidity, length of stay and cost between KTR and non-KTR undergoing appendectomy, we studied a large population of patients undergoing this procedure using the National Inpatient Sample. We also investigated the effect of receiving surgical care at a transplant center on approach and post-operative outcomes.

METHODS

Study population

We studied 1336 adult KTR and 2,640,247 non-KTR undergoing appendectomy for appendicitis from January 1, 2000 - December 31, 2011. We included all patients who had International Classification of Disease, Ninth Revision (ICD-9) procedure codes for laparoscopic or open appendectomy and an ICD-9 diagnosis codes for appendicitis. KTR were distinguished from non-KTR by the presence of ICD-9 diagnosis codes consistent with prior KT. We excluded patients with ICD-9 codes indicating a history of other solid or non-solid organ transplants (Appendix B).

Data Source

Patients were drawn from the Nationwide Inpatient Sample (NIS). Available through the Health Care Cost and Utilization Project, the NIS contains data from approximately 7 million hospital stays yearly and is made up of a stratified sample of 20% of the non-federal hospitals in the United States. The stratified sample is self-weighted to allow for population based estimates.[57] Information

provided in the NIS includes patient level hospital discharge data such as patient demographics, as well as diagnostic and procedural ICD9 codes for the index hospital admission. All study methods were approved by the Johns Hopkins Hospital Institutional Review Board.

Patient and Hospital Level Characteristics

In addition to examining basic demographic information of the study population and surgical approach (laparoscopic vs open), the Charlson Comorbidity Index score was calculated for each patient.[58,59] Hospital characteristics examined included standard NIS categories of location (rural or urban), size (small, medium, large), teaching status, and region (north east, mid-west, south, or west). In addition, we categorized hospitals as transplant centers or non-transplant centers, where a transplant center was defined as a hospital where kidney transplants were performed during the study period.

Surgical Outcomes

Between-group characteristics were compared using chi-squared tests for categorical variables and t-tests for continuous variables. We defined peri-operative mortality as a death during the index hospital admission. Peri-operative morbidity, defined as the occurrence of intraoperative or postoperative complications during the index hospital admission, was identified by ICD9 code and categorized into system-based groups as established in previous studies (Appendix E).[26] Multi-level (hierarchical) regression models with random intercepts for each hospital were adjusted for patient-level (sex, age, African American race, Charlson Comorbidity Index, primary insurance status, and surgical approach) and hospital-level factors (location, size, region, teaching status, and transplant center status). Complication rates were compared using hierarchical logistic regression. Length of stay was examined using hierarchical negative binomial regression. A mixed linear regression model was

used to examine log transformed costs, which were determined using the NIS cost-to-charge ratio files.

Transplant Center

We investigated whether the association of KTR status with mortality, morbidity, LOS and cost varied by treatment at transplant centers vs. non-transplant centers. To evaluate the effect of transplant center type on the relationship of KTR and the outcomes above, we created an interaction term for KTR status with transplant center status in the regression models described above.

Statistical Analysis

Confidence intervals are reported as per the method of Louis and Zeger.[36] Statistical analysis was performed using Stata 14.0 (StataCorp, College Station, Texas). For all analyses, a two-tailed p-value of < 0.05 was considered statistically significant.

RESULTS

Study Population

Out of 2,641,583 appendectomies performed for appendicitis during the study period, 1336 (0.05%) were done in KTR. KTR were older (46.5 vs 40.6 years, $p < 0.001$), more likely to be African American (13.6 vs 7.0%, $p < 0.001$), carried a greater comorbidity burden as reflected by a higher Charlson Comorbidity Index score (28.6% vs 4% with score ≥ 2, $p < 0.001$), less likely to be female (41.6 vs 47.1%, p 0.07), and less likely to have private insurance (40.6 vs 60.6%, $p < 0.001$). Nearly half (49.6%) of all appendectomies performed on KTR were performed at one of the 222 hospitals

identified as transplant centers, whereas only 13% of non-KTR had appendectomies at transplant centers (Table 1).

Mortality and Morbidity

Among KTR, there were no in-hospital deaths following appendectomy, compared to a 0.2% incidence in non-KTR (p = 0.5). The crude rate of overall morbidity was 17% for KTR vs 11.6% for non-KTR (p = 0.003). Specifically, KTR had higher rates of wound complications (2.5% vs 0.5%, p <0.001), infectious complications (4.9% vs 1.7%, p<0.001), and pulmonary complications (4.3% vs 1.7%, p<0.001) (Table 2). However, after adjusting for patient and hospital level factors, the odds of overall morbidity were the same comparing KTR vs non-KTR (aOR $_{0.77}1.12_{1.61}$), although the odds of infectious (aOR $_{1.24}2.24_{4.08}$), pulmonary (aOR $_{1.01}1.97_{3.81}$), and mechanical wound complications (aOR $_{1.54}3.54_{8.09}$) were still significantly higher for KTR (Table3).

Length of Stay and Cost

Median length of stay was 3 days in KTR vs 2 days in non-KTR (p <0.001) (Table 2). After adjusting for patient and hospital level characteristics including operative approach, LOS was 1.31-fold longer for KTR (ratio $_{1.19}1.31_{1.45}$) (Table 3). The average cost for appendectomy was $9,175 for KTR and $6,806 for non-KTR (p <0.001). After adjusting for patient and hospital level characteristics including operative approach, cost was 1.17-fold higher for KTR (ratio $_{1.11}1.17_{1.26}$).

Surgical Approach

Appendectomy was performed laparoscopically in 44.8% of KTRs compared to 54.4% of non-KTRs (p = 0.002). KTR had significantly more complications following open appendectomy than non-

KTR (22.4% vs 14.8%, p 0.009), but a similar complication rate following laparoscopic approach (10.6% vs 8.7%, p 0.5) (Table 4). Comparing laparoscopic and open approach in KTR only, there were significantly fewer wound (0% vs 4.6%, p 0.016) and gastrointestinal (3.2% vs 9.9%, p 0.03) complications following laparoscopic approach (Table 5). Compared to non-KTR, KTR had longer LOS following both laparoscopic (3 vs 2 days, p <0.001) and open approaches (4 vs 3 days, p <0.001). Additionally, cost was higher for KTR following both laparoscopic and open procedures when compared to non-KTR (lap $8676 vs $7063, p <0.001; open $9901 vs $6308, p <0.001) (Table 4).

Transplant Center Status

After controlling for patient and hospital level factors, KTR were significantly less likely to have a laparoscopic procedure at transplant centers than non-KTR (aOR $_{0.36}0.55_{0.85}$). When treated at transplant centers, KTR had similar morbidity to non-KTR (aOR $_{0.44}0.79_{1.43}$). The association of KTR status and length of stay differed among appendectomy patients who were cared for at transplant centers compared to non-transplant centers (p<0.001), such that among patients who underwent appendectomy at transplant centers, KTR had a 1.36-fold longer LOS compared to non-KTR. Among those at non-transplant centers, there was no association with KTR status and LOS. Additionally, after adjustment, the association of KTR status and hospital cost differed among patients who were cared for at transplant centers compared to non-transplant centers (p=0.004), such that among patients who underwent appendectomy at transplant centers, KTR had a 1.29-fold higher cost compared to non-KTR. (Table 6).

DISCUSSION

As the largest national study of kidney transplant recipients undergoing appendectomy, we report that KTR have similar mortality (0% vs 0.2%) and overall morbidity (17.0% vs 11.6% in-hospital complication rate) as non-KTR. However, KTR are more susceptible to wound (aOR $_{1.54}3.54_{8.09}$), infectious (aOR $_{1.24}2.24_{4.08}$), and pulmonary complications (aOR $_{1.01}1.97_{3.81}$) than non-KTR. While KTR had significantly longer LOS (ratio 1.37) and higher cost (ratio 1.29) than non-KTR at transplant centers, there was no difference in cost or length of stay between KTR and non-KTR at non-transplant centers.

We found that 0.05% of appendectomies for appendicitis were performed in KTR. Estimates of the incidence of appendectomy in solid organ transplant recipients is similar with reports ranging from 0.18% to 0.29%.[9,48] Our finding of no mortalities in KTR in the NIS was consistent with low mortality published in case reports and small series on appendectomy in KTR[9,48–51,54]. Further, we found that there was not a higher complication rate overall for KTR compared to non-KTR undergoing appendectomy. The largest single-center series of 17 cases of appendicitis in solid organ recipients reported a post-appendectomy complication rate of 24%[48], similar to the 17% complication rate in KTR in our study. These findings support our hypothesis that although KTR have been shown to have higher morbidity and mortality following abdominal surgery[55], appendectomy does not follow this pattern.[2,3]

We found that KTR suffered more wound, infectious, and pulmonary complications. This is likely influenced by immunosuppression. The impact of immunosuppression on wound healing and increased risk of infection is well documented in the literature, particularly in the immediate post-transplant setting.[60–63] Even with modern immunosuppressant regimens including agents such as mycophenolate mofetil and tacrolimus, higher rates of wound healing and infectious complications have been documented in KTR.[64–66]

We found that KTR have a 1.3-fold longer LOS than non-KTR, with a longer median LOS for both laparoscopic appendectomy (KTR 3 days, non-KTR 2 days) and open appendectomy (KTR 4 days, non-KTR 3 days) as compared to the median 1 day LOS that Ingraham et al. reported in their study of National Surgical Quality Improvement Project (NSQIP) data.[6] This might be influenced by the use of laparoscopy. We found that the rate of use of laparoscopy was much lower in both KTR (44.8%) and non-KTR (54.6%) in our study population compared to 76% laparoscopic appendectomy from the NSQIP database.[6] Importantly, we found that complication rates for laparoscopic appendectomy were not higher than for open appendectomy in KTR, confirming the findings of small case series.[7,8] This suggests that laparoscopic appendectomy is safe for appropriately selected KTR, and although this has been alluded to, this has not been demonstrated previously in a qualitative manner. Additionally, we report costs ranging from $6,000-9,000. A prior study of total hospital charges for appendectomy, which are higher than costs, reported a range of total charges from $20,000 to nearly $39,000.[5] While we found that KTR had significantly higher cost than non-KTR, we were limited by the nature of our study data in more granular examination of costs.

Despite the sentiment expressed in multiple opinion pieces including book chapters and editorials, there is no evidence demonstrating improved outcomes for transplant recipients at transplant centers.[24,30] Indeed, we found no difference in morbidity and mortality between KTRs treated at transplant centers and non-transplant centers, however, we did find an increase in length of stay and cost at transplant centers. This suggests surgeons are making appropriate choices in who they treat at non-transplant centers, and in treating transplant recipients at non-transplant centers, are making safe, cost-effective decisions.

This study has a few limitations which warrant further discussion. An important limitation is the lack of clinical granularity of NIS data. For example, the NIS does not include information on transplant laterality or history of multiple previous KTR, therefore we were not able to adjust for these potential confounders. Additionally, without more detailed information on the specific costs and events occurring during a hospital stay, we are unable to determine the underlying reasons for cost and length of stay differences between KTR and non-KTR, and between transplant centers and non-transplant centers. We were unable to determine whether, for example, those KTR presenting to non-transplant centers who were sicker were transferred to transplant centers for care. An additional limitation inherent in the design of the NIS is the lack of linkage of patients across multiple hospitalizations. The magnitude of the NIS, however, offers an understanding of the national outcomes of surgically treated appendicitis in KTR and avoids the bias and limited power associated with single-center studies. Finally, there has been a recent surge in non-operative management of appendicitis, however we cannot reliably assess this using the NIS, so we limited our study to operative management. It is possible that non-operative management is applied to KTR and non-KTR differently, and would make operatively managed groups less comparable in terms of disease severity.

In conclusion, we report that kidney transplant recipients have similar rates of overall complications when compared to non-transplant recipients. Despite similar complication rates, appendectomy at transplant centers is associated with longer LOS and higher cost for KTR, but it is unclear what is driving these differences. Our findings suggest that if surgeons choose to perform appendectomy at non-transplant centers, it is safe and cost effective.

Table 1. Characteristics of the study population and procedure details following appendectomy.

	KTR (n=1,336)	Non-KTR (n=2,640,247)	p-value
Age, mean (SD)	46.5 (13.0)	40.6 (16.6)	<0.001
Female, %	41.6	46.9	0.07
African American, %	13.6	6.9	<0.001
Charlson Comorbidity Index, %			<0.001
0	43.8	85.0	
1	27.6	10.9	
≥2	28.6	4.1	
Insurance Status, %			<0.001
Public	57.2	21.2	
Private	40.6	60.7	
Other	2.3	18.3	
Laparoscopic, %	44.8	54.4	0.002
Performed at transplant center, %	49.6	13.0	<0.001

Table 2. Unadjusted outcomes following appendectomy in kidney transplant recipients (KTR) vs non-KTR.

Outcome	KTR (n = 1336)	Non-KTR (n = 2,640,247)	P value
Mortality (%)	0	0.2	0.5
Any Complication (%)	**17.0**	**11.6**	**0.003**
System specific complications^ (%)			
Wound	**2.5**	**0.5**	**<0.001**
Infection	**4.9**	**1.7**	**<0.001**
Pulmonary	**4.3**	**1.7**	**<0.001**
Cardiovascular	0	0.5	0.3
Genitourinary	1.1	0.6	0.3
Gastrointestinal	6.9	7.1	0.9
Intraoperative	1.4	0.8	0.2
LOS, median days (IQR)	**3 (2-6)**	**2 (1-4)**	**<0.001**
Cost, median $ (IQR)	**9,175 (6,715-13,915)**	**6,802 (5,076-9,358)**	**<0.001**

^see Appendix E for breakdown of complications by system

Table 3. Adjusted outcomes following appendectomy in kidney transplant recipients (KTR) vs non-KTR*.

Outcome	KTR vs Non-KTR	95% CI
Any complications, OR	1.12	0.77-1.61
System specific complications^, OR		
Wound	**3.54**	**1.54-8.09**
Infection	**2.24**	**1.24-4.08**
Pulmonary	**1.97**	**1.01-3.81**
Genitourinary	1.18	0.29-4.82
Gastrointestinal	0.75	0.44-1.28
Intraoperative	1.23	0.39-3.86
LOS, ratio	**1.31**	**1.19-1.45**
Cost, ratio	**1.17**	**1.11-1.26**

*adjusted for age, race, gender, Charlson comorbidity score, insurance status, operative approach, hospital bed size, hospital region, teaching status, transplant center status
^see Appendix E for breakdown of complications by system

Table 4. Unadjusted outcomes following laparoscopic vs open appendectomy in kidney transplant recipients (KTR) and non-KTR.

Outcome	KTR (n = 1336)	Non-KTR (n = 2,640,247)	p value
Any Complication (%)	17.0	11.6	0.003
Laparoscopic	10.6	8.7	0.5
Open	22.4	14.8	0.009
LOS, median days (IQR)	3 (2-6)	2 (1-4)	<0.001
Laparoscopic	3 (1-4)	2 (1-3)	<0.001
Open	4 (2-7)	3 (2-5)	<0.001
Cost, median $ (IQR)	9,175 (6,715-13,915)	6,802 (5,076- 9,358)	<0.001
Laparoscopic	8,676 (6,575-11,524)	7,063 (5,520-9,230)	<0.001
Open	9,901 (6,787-15,832)	6,308 (4,496-9,627)	<0.001

^see Appendix E for breakdown of complications by system

Table 5. Unadjusted outcomes following laparoscopic vs open appendectomy in kidney transplant recipients ONLY.

Outcome	Laparoscopic (n = 599)	Open (n = 737)	P value
Performed at transplant center (%)	**40.7**	**59.3**	**0.003**
Any complications (%)	**10.6**	**22.4**	**0.009**
System specific complications^ (%)			
Wound	**0**	**4.6**	**0.016**
Infection	4.1	5.9	0.5
Pulmonary	2.6	5.7	0.2
Cardiovascular	0	0	1.0
Genitourinary	0.8	1.3	0.7
Gastrointestinal	**3.2**	**9.9**	**0.03**
Intraoperative	0.8	2.0	0.4
LOS, median days (IQR)	**3 (1- 4)**	**4 (2-7)**	**<0.001**
Cost, median $ (IQR)	8,676 (6575 – 11524)	9,901 (6787-15,832)	0.07

^see Appendix E for breakdown of complications by system

Table 6. Adjusted outcomes of kidney transplant recipients vs. non-transplant patients by center type.

Outcome	Transplant center	Non-transplant center	p-value for interaction
Any complications, OR	0.95 (0.54-1.67)	1.23 (0.75-2.0)	0.5
LOS, ratio	**1.36 (1.22-1.55)**	0.96 (0.84-1.08)	**<0.001**
Cost, ratio	**1.29 (1.19-1.41)**	1.01 (0.93-1.10)	**0.004**
Laparoscopic approach, OR	**0.55 (0.36-0.85)**	0.79 (0.51-1.21)	0.2

Chapter 4. Complications, Length of Stay, and Cost of Cholecystectomy in Kidney Transplant Recipients

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ABSTRACT

Background: Kidney transplant recipients (KTR) are at increased risk of requiring cholecystectomy. Given the physiologic impacts of years of renal replacement and lifelong immunosuppression, cholecystectomy may have higher risk in this unique population.

Methods: Using the National Inpatient Sample, we compared 7,318 KTR and 5,341,427 non-KTR following cholecystectomy from 2000-2011, and investigated outcomes of mortality, morbidity, length of stay (LOS) and cost, adjusting for patient and hospital level factors.

Results: For KTR compared to non-KTR, mortality (2.7% vs 1.2%, $p<0.001$) and morbidity (18.8% vs 13.9%, $p<0.001$; aOR 1.30 95%CI 1.12-1.51) were higher. LOS and costs were also greater (LOS ratio 1.23 95%CI 1.17-1.28; cost ratio 1.13 95%CI 1.08-1.17). When comparing outcomes at transplant and non-transplant centers, there were no differences.

Conclusions: KTR have higher mortality and morbidity, longer LOS, and greater peri-operative cost following cholecystectomy. It is safe and cost effective for surgeons to choose to perform cholecystectomy at non-transplant centers. Physicians should consider the elevated risks when planning for surgery in KTR and counsel patients accordingly.

INTRODUCTION

Cholecystectomy is one of the most common general surgery procedures performed in the United States, with more than 400,000 cases performed every year.[9,10] One unique patient population at increased risk for need of cholecystectomy are kidney transplant recipients (KTR). KTR are at higher risk of developing gallstones and biliary disease than the general population due to their history of renal failure and immunosuppressive medications such as calcineurin inhibitors.[14,15] This risk, combined with improved post-transplant survival, translates to a higher incidence of cholecystectomy in the kidney transplant population.[9,14] While post-cholecystectomy morbidity and mortality are low and the average hospital length of stay (LOS) is two days in the general population, it is unclear if the risks are elevated for KTR.[11–13] An improved understanding of morbidity, LOS, and associated cost in this population is important for peri-operative planning and risk stratification.

Previous single-center studies have reported that post-operative outcomes for solid organ transplant recipients following general surgical procedures are worse than the non-transplant recipients, with a recent review citing up to 32.7% morbidity and 17.5% mortality for emergency abdominal surgery, in comparison to 9% morbidity in non-transplant recipients.[6,9] For cholecystectomy specifically, a national study of solid organ transplants, including heart, lung, and liver recipients, found a complication rate of 13.6% following cholecystectomy, compared to 4.9% for non-transplant recipients .[9,11] Additionally, these heterogeneous solid-organ transplant recipients had a LOS of 4-8 days, compared to a median 1 day reported for non-transplant recipients.[11,22] Specifically regarding kidney transplant recipients, the largest case-series of cholecystectomies to date reported outcomes of 17 procedures performed in a cohort of 1,608 KTR at a single transplant center, with a mortality rate of 5.9%.[14] Given concerns of increased operative risks, many transplant providers feel that morbidity, LOS and cost might be mitigated if transplant recipients receive their surgical care at transplant centers.[24,25,30]

To explore post-cholecystectomy outcomes in a more generalizable fashion, we used the National Inpatient Sample (NIS) to investigate the differences in mortality, morbidity, LOS and cost between KTR and non-KTR undergoing cholecystectomy in a large population of patients undergoing cholecystectomy in the United States. We also investigated post-operative outcomes based on the location of surgical care at transplant centers compared to non-transplant centers.

METHODS

Data Source

Patients were drawn from the National Inpatient Sample (NIS). Available through the Healthcare Cost and Utilization Project, the NIS contains data from approximately 7 million hospital stays yearly, and is made up of a stratified sample of 20% of the non-federal hospitals in the United States. The stratified sample is self-weighted to allow for population based estimates.[57] Information provided in the NIS includes patient level hospital discharge data such as patient demographics, as well as diagnostic and procedural ICD-9 codes for the index hospital admission. All study methods were approved by the Johns Hopkins Hospital Institutional Review Board.

Study population

We studied 7,318 adult KTR and 5,341,427 non-KTR undergoing cholecystectomy from January 1, 2000 - December 31, 2011. We included all patients who had International Classification of Disease, Ninth Revision (ICD-9) procedure codes for laparoscopic or open cholecystectomy KTR were distinguished from non-KTR by the presence of ICD-9 diagnosis codes consistent with prior KT. We excluded patients with ICD-9 codes indicating a history of other solid or non-solid organ transplants (Appendix C).

Patient and Hospital Level Characteristics

In addition to examining basic demographic characteristics and surgical approach (laparoscopic vs. open), the Charlson Comorbidity Index score was calculated for each patient.[58,59] Hospital characteristics examined included standard NIS categories of location (rural or urban), size (small, medium, large), teaching status, and region (Northeast, Midwest, South, or West). We categorized hospitals as transplant centers or non-transplant centers. We defined a transplant center as a hospital where at least one kidney transplant was performed during the study period.

Clinical Outcomes

We defined peri-operative mortality as death during the primary surgical hospital admission. Peri-operative morbidities, defined as intraoperative or postoperative complications during the index hospital admission, were identified by ICD-9 code and categorized into system-based groups as established in previous studies (Appendix E).[26]

Mortality and complication rates were modeled using hierarchical logistic regression. Length of stay was examined using hierarchical negative binomial regression. Mixed linear regression was used to examine log-transformed costs, which were determined using the NIS cost-to-charge ratio files.

All models included random intercepts for each hospital and were adjusted for patient characteristics (sex, age, African American race, Charlson Comorbidity Index, primary insurance status), hospital factors (location, size, region, teaching status, and transplant center status), and surgical approach (laparoscopic or open).

Effect Modification by Transplant Center

We investigated whether the association of KTR status with mortality, morbidity, LOS and cost varied by treatment at transplant centers vs. non-transplant centers. To evaluate the effect of transplant center type on the relationship of KTR and the outcomes above, we created an interaction term for KTR status with transplant center status in the regression models described above.

Statistical Analysis

We used $\chi 2$ tests to evaluate categorical variables and Student's t test for continuous variables to compare KTR with non-KTR. For all analyses, a two-tailed p-value of < 0.05 was considered statistically significant. Confidence intervals are reported as per the method of Louis and Zeger.[36] Statistical analysis was performed using Stata 14.0 (StataCorp, College Station, Texas).

RESULTS

Study Population

A total of 7,318 KTR and 5,341,427 non-KTR underwent cholecystectomy during the study period. KTR were a similar age (52.9 vs 53.9 years, p=0.051), more likely to be male (55.3 vs 34.3%, p<0.001), African American (13.8 vs 9.3%, p <0.001), have public insurance (66.8% vs 46.3%, p <0.001) and had a higher Charlson Comorbidity Index scores (36.4% vs 16.9% with score ≥2) compared to non-KTR. KTR were less likely to have a laparoscopic cholecystectomy (68.2% vs 77.7%, p<0.001, Table 1).

Mortality and Morbidity

Mortality was higher following cholecystectomy during the index admission for KTR compared to non-KTR (2.7% vs 1.2%, p <0.001, Table 2). After adjusting for patient and hospital characteristics, the odds of mortality following cholecystectomy in KTR was 2.39-fold higher than non-KTR (aOR $_{1.66}2.39_{3.44}$). KTR were more likely than non-KTR to have postoperative complications during their surgical hospitalization (18.8% vs 13.9%, p<0.001). KTR had more wound complications (2.0% vs 0.8%, p <0.001), infectious complications (4.4% vs 2.1%, p<0.001), genitourinary complications (1.4% vs 0.8%, p=0.01) and intraoperative complications (3.7% vs 2.4%, p=0.001) than non-KTR. After adjustment, the odds of any morbidity were 1.3-fold higher in KTR than non-KTR (aOR $_{1.12}1.30_{1.51}$). KTR had 1.9-fold higher odds of wound complications (aOR $_{1.27}1.90_{2.84}$) and infectious complications (aOR $_{1.44}1.89_{2.48}$), as well as significantly higher odds of intraoperative (aOR $_{1.03}1.39_{1.86}$) complications as well when compared to non-KTR (Table 2).

Length of Stay and Cost

Median LOS was longer in KTR compared to non-KTR (5 days vs 3 days, p <0.001, Table 2). After adjusting for patient and hospital level characteristics including operative approach, LOS was 1.23-fold longer for KTR (ratio $_{1.17}1.23_{1.28}$). The median cost for cholecystectomy was $12,077 for KTR and $9,002 for non-KTR (p <0.001). Following adjustment, cost was 1.13-fold higher for KTR than non-KTR (ratio $_{1.08}1.13_{1.17}$, Table 2).

Transplant Center

KTR were more likely to be treated at kidney transplant centers than non-KTR (54.6% vs 16.8%, p >0.001, Table 1). There was no difference in mortality for KTR vs non-KTR treated at transplant centers compared to those treated at non-transplant centers (aOR: $_{1.48}2.45_{4.04}$ vs $_{1.36}2.31_{3.93}$; interaction p=0.9, Table 3). There was no difference in odds of overall complications (aOR: $_{1.00}1.24_{1.52}$ vs

$_{1.11}1.37_{1.69}$, interaction p=0.5), LOS (ratio: $_{1.18}1.25_{1.32}$ vs $_{1.14}1.21_{1.28}$, interaction p=0.4), or cost (ratio: $_{1.07}1.13_{1.18}$ vs ratio$_{1.09}1.15_{1.21}$, interaction p=0.7), when comparing treatment at transplant centers and non-transplant centers for KTR vs non-KTR (Table 3).

DISCUSSION

As the largest national study of kidney transplant recipients undergoing cholecystectomy, we found that KTR had 2.4-fold higher mortality and 30% higher overall morbidity when compared to non-KTR. KTR were more susceptible to wound (aOR 1.90), infectious (aOR 1.89), and intraoperative complications (aOR 1.39) than non-KTR. KTR had 23% longer LOS and 13% higher cost than non-KTR ($p<0.001$). These associations did not vary between transplant centers and non-transplant centers.

We found 2.7% mortality in KTR, with 2.4-fold higher odds after adjusting for multiple patient and hospital characteristics, concordant with previous single-institution studies of 0-5.9% mortality in KTR. Our findings from a larger, more generalizable cohort, support that cholecystectomy is inherently higher risk for KTR than non-KTR, independent of other patient, hospital, and procedure specific variables.[14,16] Further, we found the rate of overall complications to be significantly higher in KTR. These findings are consistent with reported morbidity in 12.5% KTRs after cholecystectomy.[67] Specifically, we found that KTR suffered more wound, infectious, and intraoperative complications than non-KTR. Although the underlying cause for this increase in complications is multifactorial, it is certainly influenced by immunosuppression of KT recipients. The impact of immunosuppression on wound healing and infection is well documented, particularly in the immediate post-transplant setting.[60,63,65,66] Even with improved immunosuppressant regimens, higher rates of wound healing issues and infectious complications have been documented in KTR.[62] Additionally, the global tissue

damage caused by years of renal failure and/or dialysis might increase intraoperative complications as well.[68,69]

We found the median LOS for KTR to be significantly longer than non-KTR (5 vs 3 days). We report a shorter median LOS than previous studies of solid organ transplant recipients undergoing cholecystectomy (9 days)[9], but similar LOS to other reports for the general population (1-3 days).[11] Additionally, we report significantly higher cost for KTR compared to non-KTR. A recent study reported median cost of cholecystectomy in the general population ranging from $8,552 to $13,526 for average length hospital stays, which is similar to our finding of $9,002 for non-transplant recipients.[18] However, median cost for KTR was 13%% higher following adjustment. Although this difference is significant, the nature of our study data precluded a more granular examination of costs.

Despite the sentiments expressed in multiple opinion pieces including book chapters and editorials, we did not find better outcomes for transplant recipients at transplant centers.[24,30] While there was a significantly higher percentage of cholecystectomies performed at transplant centers in the KTR population (54.6%) compared to the non-KTR group (16.8%), the mortality, morbidity, LOS and cost were similar for KTR regardless of location of care. This suggests that cholecystectomies are safe and cost effective at non-transplant centers when surgeons feel comfortable treating KTR.

Although laparoscopic cholecystectomy has evolved to become the surgical approach of choice for gallbladder surgery and a history of kidney transplantation is not considered a contraindication to laparoscopic cholecystectomy, we found a nearly 10% difference in the application of laparoscopic approach for KTR.[7,16] This is consistent with a recent review that demonstrated laparoscopic

approach in 72% of cholecystectomy cases in transplant recipients, compared to 89.5% laparoscopic approach in the general population.[9,11]

This study has some limitations which warrant further discussion. An important limitation is the lack of clinical granularity of NIS data. While the admitting diagnosis is routinely recorded and helpful in determining the indication for surgery, it is often vague. Therefore, we were unable to control for cholecystectomy indication. Without detailed information on the specific costs and events occurring during a hospital stay, we are also unable to determine the underlying reasons for cost and length of stay differences between KTR and non-KTR. For example, we were unable to determine whether those KTR presenting to non-transplant centers that were sicker were transferred to transplant centers for care. An additional limitation inherent in the design of the NIS is the lack of linkage of patients across multiple hospitalizations, thereby limiting ability to comment on later graft or patient outcomes. The magnitude of the NIS, however, offers insight into national outcomes of cholecystectomy in KTR and avoids the bias and limited power associated with single-center studies.

In conclusion, we report that kidney transplant recipients have higher mortality, greater morbidity, longer LOS and higher cost when compared to non-transplant recipients undergoing cholecystectomy, regardless of location of care. Cholecystectomies are as safe and cost effective at non-transplant centers as they are at transplant centers if surgeons feel comfortable treating KTR. Our findings suggest that surgeons should consider these elevated risks when planning for surgery in the KTR population, counsel patients accordingly, and monitor vigilantly for post-operative complications.

Table 1. Characteristics of the study population, hospital and procedure details for kidney transplant recipients (KTR) and non-KTR undergoing cholecystectomy between 2000-2011.

	KTR (n= 7,318)	Non-KTR (n= 5,341,427)	p-value
Age, mean (SD)	52.9 (13.5)	53.9 (19.1)	0.051
Male, %	55.3	34.3	<0.001
African American, %	13.8	9.3	<0.001
Charlson Comorbidity Index, %			<0.001
0	35.5	61.7	
1	28.1	21.4	
≥2	36.4	16.9	
Insurance Status, %			<0.001
Public	66.8	46.3	
Private	30.0	42.5	
Other	2.2	11.2	
Laparoscopic, %	68.2	77.7	<0.001
Performed at transplant center, %	54.6	16.8	<0.001

Table 2. Unadjusted and adjusted* outcomes following cholecystectomy in kidney transplant recipients (KTR) vs non-KTR.

	Unadjusted			Adjusted*	
Outcome	KTR (n = 7318)	Non-KTR (n = 5,341,427)	p value	KTR vs Non-KTR	95% CI
Mortality, %	**2.7**	**1.2**	**<0.001**	**2.39**	**1.66-3.44**
Any Complication, %	**18.8**	**13.9**	**<0.001**	**1.30**	**1.12-1.51**
System specific complications,^ %					
Wound	**2.0**	**0.8**	**<0.001**	**1.90**	**1.27 -2.84**
Infection	**4.4**	**2.1**	**<0.001**	**1.89**	**1.44-2.48**
Pulmonary	3.3	3.3	0.9	0.99	0.72-1.35
Cardiovascular	1.2	1.2	0.9	0.89	0.51-1.54
Genitourinary	1.4	0.8	0.01	1.48	0.91-2.41
Gastrointestinal	5.9	5.8	0.8	0.88	0.69-1.12
Intraoperative	**3.7**	**2.4**	**0.001**	**1.39**	**1.03-1.86**
LOS, median days (IQR)	**5 (3-9)**	**3 (2-6)**	**<0.001**	**1.23**	**1.17-1.28**
Cost, median $ (IQR)	**12,077 (7,717-19,766)**	**9,002 (6,182-13,886)**	**<0.001**	**1.13**	**1.08-1.17**

*adjusted for age, race, gender, Charlson comorbidity score, insurance status, hospital bed size, hospital region, teaching status, surgical approach

^see Appendix E for breakdown of complications by system

Table 3. Adjusted outcomes of kidney transplant recipients vs. non-transplant patients by center type following cholecystectomy. *

Outcome	Transplant center	Non-transplant center	p-value for interaction
Mortality, OR	2.45 (1.48 - 4.04)	2.31 (1.36 - 3.93)	0.9
Any complications, OR	1.24 (1.00 - 1.52)	1.37 (1.11 - 1.69)	0.5
LOS, ratio	1.25 (1.18-1.32)	1.21 (1.14 - 1.28)	0.4
Cost, ratio	1.13 (1.07-1.18)	1.15 (1.09-1.21)	0.7

*adjusted for age, race, gender, Charlson comorbidity score, insurance status, hospital bed size, hospital region, teaching status, surgical approach

Chapter 5. Outcomes Following Colorectal Resection in Kidney Transplant Recipients

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ABSTRACT

Purpose: Kidney transplant recipients (KTR) are at increased risk of requiring colorectal resection compared to the general population. Given the need for lifelong immunosuppression and the physiologic impact of years of renal replacement, we hypothesized that colorectal resection may be riskier for this unique population.

Methods: We investigated the differences in mortality, morbidity, length of stay (LOS), and cost between 2,410 KTR and 1,433,437 non-KTR undergoing colorectal resection at both transplant and non-transplant centers using the National Inpatient Sample between 2000-2013, adjusting for patient and hospital level factors.

Results: In hospital mortality was higher for KTR in comparison to non-KTR (11.1 vs 4.3%, $p<0.001$; adjusted odds ratio [aOR] $_{2.68}3.59_{4.81}$) as were overall complications (38.5 vs 31.5%, $p=0.001$; aOR $_{1.08}1.30_{1.56}$). LOS was significantly longer (10 vs 7 days, $p<0.001$; ratio $_{1.42}1.53_{1.65}$) and cost was significantly greater ($23,056 vs $14,139, $p<0.001$; ratio $_{1.42}1.54_{1.63}$) for KTR compared to non-KTR. While LOS was longer for KTR undergoing resection at transplant centers compared to non-transplant centers (aOR 1.68 vs 1.53, $p=0.03$), there were no statistically significant differences in mortality, overall morbidity, or cost by center type.

Conclusions: KTR have higher mortality, higher incidence of overall complications, longer LOS, and higher cost than non-KTR following colorectal resection, regardless of center type. Physicians should consider these elevated risks when planning for surgery in the KTR population and counsel patients accordingly.

Keywords: general surgery, kidney transplantation, colorectal resection, colectomy

INTRODUCTION

More than 300,000 colectomies are performed in the annually in the United States for a variety of pathologies, including diverticulitis and cancer.[17,18] Because transplant recipients are at increased risk of these diseases, they are more likely to require colorectal resections compared to the general population. For example, transplant recipients have 2.6x higher incidence of colorectal cancer than non-transplant recipients[19], with a 5-year cumulative incidence rate of 0.5%.[20] Kidney transplant recipients (KTR) also have a higher incidence of acute diverticulitis than the general population (0.94% vs 0.02%).[21] Furthermore, as post-transplant survival improves and the KTR population ages, the number of KTR requiring colorectal resection will increase proportionally.[55,56] An improved understanding of mortality, morbidity, length of stay, and associated cost of colorectal resection in this population is important for peri-operative planning and risk stratification.

A systematic review of single-institution studies of immunosuppressed patients demonstrated a 23% mortality rate for colorectal resection for diverticulitis[21], while another found 17.5% mortality following resection for colonic perforation[9], both significantly higher than anticipated in the general population.[17] As with other types of general surgery in KTR, single-institution case series have demonstrated a prolonged length of stay (LOS) following colorectal resection, with one study reporting a median LOS of 22.2 days compared to a national average of 9.3 days for open colectomy.[9,26,70] Given concerns of increased operative risk, it has been suggested that any increased morbidity, LOS or cost might be reduced if transplant recipients receive their surgical care at transplant centers.[24,25,30]

We used the National Inpatient Sample (NIS), a large, nationally representative database, to investigate the differences in mortality, morbidity, length of stay and cost between KTR and non-KTR undergoing colorectal resection in the United States. We also investigated post-resection

outcomes based on the location of surgical care at transplant centers compared to non-transplant centers.

MATERIALS AND METHODS

Data Source

Patients were drawn from the NIS. Available through the Health Care Cost and Utilization Project, the NIS contains data from approximately 7 million hospital stays yearly and is made up of a stratified sample of 20% of the non-federal hospitals in the United States. The stratified sample is self-weighted to allow for population based estimates.[57] Information provided in the NIS includes patient level hospital discharge data such as patient demographics, as well as diagnostic and procedural ICD-9 codes for the index hospital admission. All study methods were approved by the Johns Hopkins Hospital Institutional Review Board.

Study Population

We studied 2,410 KTR and 1,433,437 non-KTR undergoing colorectal resections from January 1, 2000 - December 31, 2013. We limited the study to patients who had an International Classification of Disease, Ninth Revision (ICD-9) procedure code for laparoscopic or open colorectal resection and included both elective and urgent/emergent indications. KTR were distinguished from non-KTR by the presence of ICD-9 diagnosis codes consistent with prior kidney transplantation. We excluded patients with ICD-9 codes indicating a history of other solid or non-solid organ transplants (Appendix A) and patients who underwent both kidney transplantation and colorectal resection during the same hospital admission.

Patient, Hospital, and Procedure Characteristics

Basic demographic information was examined and the Charlson Comorbidity Index Score was calculated for each patient.[1,2] Hospital and procedure characteristics included standard NIS categories

of location (rural or urban), size (small, medium, large), teaching status, region (Northeast, Midwest, South, or West), surgical approach (laparoscopic vs open), case status (elective vs urgent/emergent), and calendar year. In addition, we categorized hospitals as transplant centers (a hospital where at least one kidney transplant was performed during the study period) or non-transplant centers.

Clinical Outcomes

We defined mortality as death during the primary surgical hospital admission. Morbidity, defined as intraoperative or postoperative complications during the primary surgical hospital admission, were identified by ICD-9 code and categorized into system-based groups as established in previous studies (Appendix B).[3] Incidence of mortality and morbidity were modeled using hierarchical logistic regression. Length of stay was examined using hierarchical negative binomial regression. Mixed linear regression was used to examine log-transformed costs, which were determined using the NIS cost-to-charge ratio files.

All models included random intercepts for each hospital and were adjusted for patient (sex, age, African American race, Charlson Comorbidity Index, primary insurance status) and hospital factors (location, size, region, teaching status, and transplant center status). Secular trends were evaluated by adjusting all models for calendar year. Variables for case status and surgical approach were not associated with outcomes in univariable or multivariable models; for model parity they were not included in reported models.

Effect Modification by Transplant Center

We investigated whether the association of KTR status with mortality, morbidity, LOS and cost varied by treatment at transplant centers vs. non-transplant centers. To evaluate the effect of transplant center type on the relationship of KTR and the outcomes above, we created an interaction term for KTR status with transplant center status in the regression models described above.

Statistical Analysis

We used χ^2 tests to evaluate categorical variables and Student's t test for continuous variables to draw between-group comparisons. For all analyses, a two-tailed p-value of < 0.05 was considered statistically significant. Confidence intervals are reported as per the method of Louis and Zeger.[36] Statistical analysis was performed using Stata 14.0 (StataCorp, College Station, Texas).

RESULTS

Study Population

In total, 2,410 KTR and 1,433,437 non-KTR underwent colorectal resection during the study period. KTR were younger (58.2 vs 65.1 years, p<0.001), more likely to be male (58.7% vs 46.2%, p<0.001), African American (20.2% vs 10.2%, p<0.001), have public insurance (68.4% vs 59.1%, p<0.001) and have higher Charlson Comorbidity Index scores (43.2% vs 35.7% with score ≥3). KTR were less likely to have a laparoscopic colorectal resection (20.4% vs 30.5%, p=0.002) and less likely to undergo an elective procedure (47.3% vs 61%, p >0.001) (Table 1).

Mortality and Morbidity

Mortality was higher following colorectal resection for KTR compared to non-KTR (11.1% vs 4.3%, p <0.001). After adjusting for patient and hospital characteristics, the odds of mortality following colorectal procedures in KTR was 3.59-fold higher than non-KTR (aOR $_{2.68}3.59_{4.81}$). KTR were more likely than non-KTR to have postoperative complications during their surgical hospitalization (38.5% vs 31.5%, p = 0.001). Specifically, KTR had more wound complications (6.2% vs 2.4%, p <0.001), infectious complications (7.7% vs 4.2%, p<0.001), cardiovascular complications (5.2 vs 2.7%, p<0.001), pulmonary complications (8.0% vs 5.3%, p=0.008) and intraoperative complications (6.5% vs 3.9%, p=0.003) than non-transplant recipients (Table 2). After adjustment, the odds of overall morbidity were 1.30-fold higher in KTR than non-KTR (aOR $_{1.08}1.30_{1.56}$). Specifically, KTR had

higher odds of cardiovascular (aOR $_{1.45}2.19_{3.31}$), wound (aOR $_{1.35}1.97_{2.87}$), infectious (aOR $_{1.08}1.52_{2.13}$), pulmonary (aOR $_{1.21}1.70_{2.39}$), and intraoperative (aOR $_{1.15}1.66_{2.38}$) complications when compared to non-KTR (Table 3).

Length of Stay and Cost

Median length of stay (LOS) was longer in KTR compared to non-KTR (10 days vs 7 days, p<0.001). Following adjustment, KTR had a 53% longer LOS than non-KTR (ratio $_{1.43}1.53_{1.65}$). Cost of care was higher for KTR than non-KTR, with a median difference of $9,000 dollars ($23,056 vs $14,139, p <0.001). Following adjustment, cost was 54% higher in KTR than non-KTR (ratio $_{1.42}1.53_{1.63}$) (Tables 2 & 3).

Transplant Center

KTR were more likely to be treated at kidney transplant centers than non-KTR (29.9% vs 8.9%, p >0.001) (Table 1). The association of KTR status and mortality did not differ by center type (interaction p=0.6). The association of KTR status and overall complications and most system specific complications did not differ by center type (Table 4). Among colorectal resection patients at transplant centers, there was no association between KTR status and infection. However, for colorectal resection at non-transplant centers, KTR had a 2-fold increased risk of infection compared to non-KTR (aOR $_{1.36}1.99_{2.91}$, interaction p= 0.03). Additionally, among KTR treated at transplant centers, LOS was longer than at non-transplant centers (ratio 1.68 vs 1.53, interaction p= 0.03). The association of KTR status and cost did not differ by center type (Table 4).

DISCUSSION

In this national, 14-year study of 2,410 kidney transplant recipients undergoing colorectal resection, we found that KTR had a 3.6-fold increase in mortality and 1.3-fold increase in overall morbidity when compared to non-KTR. KTR were more susceptible to wound (6.2 vs 2.4%), infectious (7.7 vs

4.2%), cardiovascular (5.2 vs 2.7%), pulmonary (8.0 vs 5.3%) and intraoperative (6.5 vs 3.9%) complications than non-KTR. Cost was 1.5-fold higher for KTR compared to non-KTR. KTR also had a 1.5-fold longer LOS than non-KTR, with an additional 15% increase in LOS when KTR are treated at transplant centers.

Our findings of significantly higher mortality in KTR undergoing colorectal resection are consistent with and expand on single-institution studies of solid organ transplant recipients which document 7 to 10% mortality rates from colorectal disease complications.[71–73] A recent national study of emergency colorectal surgery reported a 9.3% mortality rate,[17] appropriately higher than the rate we report for the non-transplant population (4%), given that our sample contains both elective and urgent/emergent surgical resections. However, considering nearly half of the transplant recipients in our study population had elective resections, the 3.6-fold increase in mortality that we report after adjustment is striking.

Furthermore, we found the rate of overall complications to be significantly higher in KTR. Specifically, we found that KTR suffered more wound, infectious, cardiovascular, pulmonary, and intraoperative complications than non-KTR. These findings are consistent with a recent systematic review of gastrointestinal complications in solid organ transplant recipients that reported a 33% incidence of complications following resection for diverticular disease, and several single institution case series reporting between 60-100% complication rate for colorectal resections for diverticulitis or lower gastrointestinal perforations.[9,55,71]

Although the underlying cause for our findings of increased mortality and complications is multifactorial, it is likely heavily influenced by immunosuppression. The impact of immunosuppression on wound healing and infection is well documented, particularly in the immediate post-transplant setting.[60,63] Even with improved immunosuppressant regimens, higher

rates of wound healing issues and infectious complications have been documented in KTR.[62,74] In addition, we have demonstrated that cardiovascular, pulmonary and intraoperative complications are more frequent in KTR. The global tissue damage caused by years of renal failure and/or dialysis is potentially responsible for an increase in complications associated with these organ systems and subsequent mortality.[69]

We found the median length of stay for kidney transplant recipients to be significantly longer than non-transplant recipients (10 vs 7 days), particularly when treated at a transplant center (11 vs 7 days). The median LOS we report for the general population is similar to other reports that document LOS of 6-9 days following open colorectal resection, as only 20% of patients in our study underwent laparoscopic approach.[18,26] Our findings are consistent with longer LOS documented in other smaller, single institutions studies of transplant recipients undergoing general surgical procedures.[70,75,76] Additionally, we reported significantly higher cost for kidney transplant recipients compared to non-transplant recipients. A recent national study of colectomy reported median costs ranging from $12,071 - 14,141 depending on surgical approach for the general population, which is similar to our finding of median cost of $14,139 for non-transplant recipients.[18] However, median cost for kidney transplant recipients was 54% higher following adjustment. While this difference is significant, the nature of our study data precluded a more granular examination of costs.

Despite the sentiments expressed in multiple opinion pieces including book chapters and editorials, we did not find better outcomes for transplant recipients at transplant centers.[24,30,32] In fact, we found that KTR had a 15% longer LOS when treated at transplant centers. Given the constellation of similar mortality, morbidity and cost in the setting of longer LOS at transplant centers, the longer LOS does not appear to be attributable to a difference in illness severity at transplant centers compared to non-transplant centers. This is potentially suggestive of more conservative discharge criteria and behavior at transplant centers.

This study has some limitations that warrant further discussion. An important limitation was the lack of clinical granularity of NIS data. While the admitting diagnosis was routinely recorded and helpful in determining the indication for surgery, it was often vague, hindering our ability to adjust for colorectal resection indication. Without detailed information on the specific costs and events occurring during a hospital stay, we were also unable to determine the underlying reasons for cost and length of stay differences between KTR and non-KTR, and between transplant centers and non-transplant centers. We were unable to determine whether, for example, those KTR presenting to non-transplant centers who were sicker were transferred to transplant centers for care. An additional limitation inherent in the design of the NIS was the lack of longitudinal follow-up across multiple hospitalizations, and the lack of linkage to transplant registries, thereby limiting our ability to study later graft or patient outcomes. The magnitude of the NIS, however, offers an understanding of the national outcomes of colorectal resections in KTR and avoids the bias and limited power associated with single-center studies. It also allows us to perform multivariable analyses, investigate interactions, and study outcomes at transplant vs non-transplant centers.

CONCLUSION

In this large national study, kidney transplant recipients had higher mortality, greater morbidity, and higher cost when compared to non-transplant recipients following colorectal resection, regardless of center type. Current patient selection practice by surgeons suggests that if surgeons feel comfortable operating, colorectal resection at non-transplant centers are as safe and as cost-effective as transplant centers, with even shorter length of stay. Our findings suggest that surgeons should consider the elevated risks when planning for surgery in the KTR population and counsel patients accordingly, but should proceed with the operation at a non-transplant center if they feel comfortable.

Table 1. Characteristics and hospital and procedure details for kidney transplant recipients (KTR) and non-KTR undergoing colorectal resection between 2000-2013.

	KTR (n=2,410)	Non-KTR (n=1,433,437)	p-value
Age, mean (SD)	58.2 (11.9)	65.1 (15.5)	<0.001
Female, %	41.3	53.8	<0.001
African American, %	20.2	10.2	<0.001
Charlson Comorbidity Index, %			<0.001
0	22.8	31.1	
1	10.2	11.8	
2	23.8	21.4	
≥3	43.2	35.7	
Insurance Status, %			<0.001
Public	68.4	59.1	
Private	29.7	36.1	
Other	1.8	4.8	
Hospital bed size, %			<0.001
Small	3.9	11.7	
Medium	20.6	24.9	
Large	75.6	63.4	
Hospital location/teaching status, %			<0.001
Rural	2.9	10.0	
Urban non-teaching	24.8	44.2	
Urban teaching	72.3	45.8	
Hospital region, %			0.5
Northeast	23.0	23.6	
Midwest	19.3	17.5	
South	37.7	40.4	
West	20.0	18.5	
Laparoscopic, %	20.4	30.5	<0.001
Performed at transplant center, %	29.9	8.9	<0.001
Elective case, %	47.3	61.0	<0.001

Table 2. Unadjusted outcomes following colorectal resection in kidney transplant recipients (KTR) vs non-KTR.

Outcome	KTR (n = 2410)	Non-KTR (n = 1,443,437)	P value
Mortality, %	11.1	4.3	<0.001
Any Complication, %	38.5	31.5	0.001
System specific complications,^ %			
Wound	6.2	2.4	<0.001
Infection	7.7	4.2	<0.001
Pulmonary	8.0	5.3	0.008
Cardiovascular	5.2	2.7	<0.001
Thromboembolic	0.4	0.3	0.7
Genitourinary	2.2	1.3	0.08
Gastrointestinal	18.4	19.3	0.6
Intraoperative	6.5	3.9	0.003
LOS, median days (IQR)	10 (6-20)	7 (5-11)	<0.001
At KT center	11 (7-24)	7 (5-12)	<0.001
At non-KT center	9 (6-18)	7 (5-11)	<0.001
Cost, median $ (IQR)	23,056 (13,408-45,217)	14,139 (9,642-23,313)	<0.001
At KT center, median $ (IQR)	21,360 (13,475-50,380)	15,615 (10,613 – 26,152)	<0.001
At non-KT center, median $ (IQR)	23,899 (13,380-43,015)	13,964 (9,547 – 23,036)	<0.001

^ see Appendix E for breakdown of complications by system

Table 3. Adjusted outcomes* following colorectal resection in kidney transplant recipients (KTR) vs non-KTR.

Outcome	KTR vs Non-KTR	95% CI
In hospital mortality, OR	**3.59**	**2.68-4.81**
Any complication, OR	**1.30**	**1.08-1.56**
System specific complications^, OR		
Wound	**1.97**	**1.35-2.87**
Infection	**1.52**	**1.08-2.13**
Pulmonary	**1.70**	**1.21-2.39**
Cardiovascular	**2.19**	**1.45-3.31**
Thromboembolic	1.22	0.30-4.95
Genitourinary	1.81	0.98-3.31
Gastrointestinal	0.91	0.72-1.15
Intraoperative	**1.66**	**1.15-2.38**
LOS, ratio	1.53	1.42-1.65
Cost, ratio	1.54	1.42-1.63

^see Appendix E for breakdown of complications by system
*adjusted for age, race, gender, Charlson comorbidity score, insurance status, hospital bed size, hospital region, teaching status, transplant center, calendar year

Table 4. Adjusted outcomes* following colorectal resection for kidney transplant recipients (KTR) vs. non-KTR by center type.

Outcome	Transplant center	Non-transplant center	p-value for interaction
Mortality, OR	3.95 (2.39-6.51)	3.43 (2.39-4.91)	0.6
Any complication, OR	1.44 (1.02-2.01)	1.24 (0.99-1.55)	0.7
System specific complications^, OR			
Wound	1.84 (1.01-3.37)	2.05 (1.27-3.33)	0.8
Infection	**0.75 (0.38-1.63)**	**1.99 (1.36-2.91)**	**0.03**
Pulmonary	1.02 (0.52-2.03)	2.12(1.43-3.14)	0.07
Cardiovascular	2.93 (1.56-5.51)	1.83(1.07-3.16)	0.3
Thromboembolic±	1.99 (0.49-8.07)	-	-
Genitourinary	2.43 (0.98-6.03)	1.49 (0.66-3.38)	0.4
Gastrointestinal	1.02 (0.67-1.57)	0.87 (0.65-1.15)	0.5
Intraoperative	1.09 (0.53-2.24)	1.99 (1.31-3.02)	0.2
LOS, ratio	**1.68 (1.50-1.87)**	**1.53 (1.43-1.65)**	**0.03**
Cost, ratio	1.50 (1.33-1.68)	1.54 (1.41-1.68)	0.8

^see Appendix E for breakdown of complications by system
*adjusted for age, race, gender, Charlson comorbidity score, insurance status, hospital bed size, hospital region, teaching status, transplant center, calendar year
±no thromboembolic events occurred at non-transplant centers

Chapter 6. Conclusion

From our nationally distributed survey, we found that the majority of surveyed acute care (AC) surgeons and transplant surgeons felt comfortable performing laparoscopic or open acute care surgery on transplant recipients. Transplant surgeons reported high comfort with these procedures despite performing fewer advanced cases in their routine practice than acute care surgeons and despite few regularly taking general surgery call. The vast majority of surgeons believed that transplant recipients receive better care at transplant centers and recommended treating transplant recipients at transplant centers whenever feasible. AC surgeons at transplant and non-transplant centers and transplant surgeons recommended that transplant recipients requiring acute care surgery who were less than 5-years post-transplant or had acute organ failure should be transferred to transplant teams or centers, respectively.

In our analysis of outcomes following appendectomy among kidney transplant recipients (KTR), we found that KTR have similar rates of overall complications when compared to non-transplant recipients. Despite similar complication rates, appendectomy for KTR at transplant centers was associated with longer LOS and higher cost than at non-transplant centers. Our findings also suggest that appendectomy in KTR at non-transplant centers is safe and cost effective.

Regarding cholecystectomy and colorectal resection, we report that kidney transplant recipients had higher mortality, greater morbidity, longer LOS, and higher cost when compared to non-transplant recipients. Despite worse outcomes among KTR following cholecystectomy, outcomes for these patients did not vary if they were treated at a transplant centers or non-transplant centers. Following colorectal resection, length of stay was, however, significantly longer for KTR at transplant centers compared to non-transplant centers; the remaining post-colorectal resection outcomes did not vary by center type.

In our national survey, we found that surgeons working at transplant centers believed the length of stay would be shorter at transplant centers, while AC surgeons at non-transplant centers believed it would be the same regardless of center type. Our retrospective analyses using the National Inpatient Sample directly contradict these surgeon beliefs. We found that LOS was longer following appendectomy and colectomy at transplant centers compared to non-transplant centers. Furthermore, the majority of surgeons surveyed believed that hospital cost would be the same for care regardless of transplant center type, however, cost following appendectomy was significantly higher at transplant centers. The disconnect between surgeon perceptions and nationally representative data could be undermining attempts to improve care for transplant recipients. For example, if surgeons believe transplant centers will provide superior care and incur similar LOS and cost for transplant recipients, they may be more inclined to transfer their transplant recipient to a transplant center, when in reality, the patient would have had a similar rate of complications at the non-transplant center and enjoy shorter LOS and lower cost.

Our findings suggest that surgeons should carefully counsel previous transplant recipients and vigilantly monitor for post-operative complications given their elevated risks of mortality and morbidity, longer LOS, and higher post-operative costs, particularly following cholecystectomy and colorectal resection. Our findings do not support the broad recommendation of transferring transplant recipients to transplant centers for acute care surgery, given largely similar rates of complications for transplant recipients between center types. Finally, our novel documentation of surgeon perceptions regarding acute care surgery in transplant recipients motivates future prospective study in the potential benefits and drawbacks of treating transplant recipients at transplant centers.

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Appendix A. Complete survey instrument

Performing General Surgical Procedures on Transplant Recipients:
Surgeon Perspectives

We would like to thank you for participating in this short survey, which should only take 3-5 minutes of your time. Our goals are to characterize the opinions and attitudes of surgeons regarding performing non-transplant surgical procedures on transplant recipients.

Your completion of this questionnaire will serve as your consent to be in this research study.
IRB00127443 Johns Hopkins University

Please indicate your number of years in practice following completion of training (residency or fellowship if applicable):

- ○ <5 (1)
- ○ 5-10 (2)
- ○ 11-20 (3)
- ○ 21+ (4)
- ○ Still in training (5)

Please indicate your personal approximate case volume per year:

- ○ <100 cases (1)
- ○ 101-200 (2)
- ○ 201-300 (3)
- ○ 300+ (4)

Please select the type of hospital at which you primarily practice:

- ○ Community (1)
- ○ Community with academic affiliation (2)
- ○ Academic/Teaching (3)
- ○ Other (4) _____

Please indicate the setting of your primary practice location:

- ○ Rural (1)
- ○ Urban (2)
- ○ Suburban (3)

Is your hospital a transplant center?

- ○ Yes (1)
- ○ No (2)

Display This Question:

If Is your hospital a transplant center? = No

How close is the nearest transplant center to you?

- ○ <10 miles (1)
- ○ 10-19 miles (2)
- ○ 20-49 miles (3)
- ○ 50-100 miles (4)
- ○ >100 miles (5)
- ○ I don't know (6)

End of Block: Demographics

Start of Block: Your Practice

Display This Question:

If Is your hospital a transplant center? = Yes

What is the scope of practice of transplant surgeons at your hospital?

- ○ Practice general surgery and perform transplants (1)
- ○ Practice general surgery ON TRANSPLANT PATIENTS ONLY and perform transplants (2)
- ○ Do not practice general surgery, ONLY perform transplants (3)
- ○ I don't know (4)

Display This Question:

If Is your hospital a transplant center? = Yes

Do you perform transplant surgery?

- ○ Yes (1)
- ○ No (2)

Display This Question:

If Do you perform transplant surgery? = Yes

Which transplant surgeries do you perform routinely? Select all that apply.

- ☐ Kidney (1)
- ☐ Liver (2)
- ☐ Pancreas (3)
- ☐ Small bowel (4)
- ☐ Other: (5)

Do you take acute care surgery, emergency general surgery, or trauma surgery call?

- ○ Yes (1)
- ○ No (2)

Which of the following cases do you perform in your current practice (select all that apply)?

- [ ] Appendectomy (1)
- [ ] Cholecystectomy (2)
- [ ] Hernia repair (3)
- [ ] Colectomy (4)
- [ ] Small bowel resection (5)
- [ ] Gastrectomy (6)
- [ ] None of the above (7)

Do you perform laparoscopic procedures, specifically appendectomy or cholecystectomy?

- ○ Yes (1)
- ○ No (2)

Display This Question:

If Do you perform transplant surgery? = No

Or Do you perform transplant surgery? , Yes Is Not Displayed

Or Do you perform transplant surgery? != Yes

Have you ever operated on a patient with a history of prior transplant?

- ○ Yes (1)
- ○ No (2)

Display This Question:

If Do you perform transplant surgery? = Yes

In your practice following completion of training, do you perform non-transplant surgery on patients with a history of prior transplant?

- ○ Yes, often (1)
- ○ Yes, occasionally (2)
- ○ Yes, rarely (3)
- ○ No (4)

End of Block: Your Practice

Start of Block: Reasonable Standard of Care- Txp Center ACS Surgeon

Display This Question:

If Is your hospital a transplant center? = Yes

And Do you perform transplant surgery? = No

If you were consulted on a transplant recipient needing an ELECTIVE operation, would you refer them to the transplant surgery team?

- ○ Yes (1)
- ○ No (2)

Display This Question:

If Do you perform transplant surgery? = Yes

If you were consulted on a transplant recipient needing an ELECTIVE general surgery operation, would you refer them to an acute care/general surgeon?

- ○ Yes, in all cases (1)
- ○ Yes, but only for complex procedures (2)
- ○ No (3)

Display This Question:

If Is your hospital a transplant center? = No

If you were consulted on a transplant recipient needing an ELECTIVE operation, would you rather refer them to a surgeon at a transplant center?

- Yes (1)
- No (2)

Display This Question:

If Is your hospital a transplant center? = Yes

And Do you perform transplant surgery? = No

If you were consulted on a transplant recipient needing an ELECTIVE operation, would you operate on the patient BUT ALSO contact a transplant surgeon for assistance?

- Always (1)
- Most of the time (2)
- Sometimes (3)
- Rarely (4)
- Never (5)

Display This Question:

If Is your hospital a transplant center? = Yes

And Do you perform transplant surgery? = No

If you were consulted on a transplant recipient needing an URGENT/EMERGENT operation, would you refer them to the transplant surgery team?

- Yes (1)
- No (2)

Display This Question:

If Is your hospital a transplant center? = No

If you were consulted on a transplant recipient needing an URGENT/EMERGENT operation, would you rather transfer them to a transplant center if possible?

- Yes (1)
- No (2)

Display This Question:

If Do you perform transplant surgery? = No

If you were consulted on a transplant recipient needing an URGENT/EMERGENT operation, would you operate on the patient BUT ALSO contact a transplant surgeon for assistance?

- Always (1)
- Most of the time (2)
- Sometimes (3)
- Rarely (4)
- Never (5)

Display This Question:

If Do you perform transplant surgery? = Yes

If you were consulted on a transplant patient needing an URGENT/EMERGENT general surgery operation, would you refer them to an acute care/general surgeon?

- Yes (1)
- No (2)

Skip To: Q19 If you were consulted on a transplant patient needing an URGENT/EMERGENT general surgery operatio... = Yes

Display This Question:

If Do you perform transplant surgery? = Yes

If you would not typically refer a transplant recipient needing an URGENT/EMERGENT general surgery operation but would rather perform the operation yourself, would you contact an acute care/general surgeon for preoperative or intraoperative assistance?

- Always (1)
- Most of the time (2)
- Sometimes (3)
- Rarely (4)
- Never (5)

Would you feel comfortable using laparoscopy on transplant recipients requiring acute care surgery procedures (appendectomy, cholecystectomy)?

- Yes (1)
- No, but I do laparoscopy on non-transplant recipients (2)
- No, but I prefer not to use laparoscopic techniques on any patients (3)
- No, because I would not feel comfortable performing acute care surgery on transplant recipients at all (4)

Display This Question:

If Is your hospital a transplant center? = No

Do you have the ability to contact a transplant center or transplant surgeon to ask for help or advice if needed?

- ○ Yes, easily (1)
- ○ Yes, but it would be difficult (2)
- ○ No (3)

Does your hospital or practice group have a policy regarding who is responsible for operating on transplant patients for non-transplant surgeries?

- ○ Yes (1)
- ○ No (2)
- ○ Unsure (3)

Display This Question:

If Is your hospital a transplant center? = Yes

At your primary hospital, who should perform urgent/emergent general surgery operations on transplant recipients?

- ○ Acute care surgeons (1)
- ○ Transplant surgeons (2)

Display This Question:

If Is your hospital a transplant center? = Yes

If patients have a history of transplant at a DIFFERENT hospital and comes to your transplant center with a need for acute care surgery, who usually performs procedures on these patients?

- ○ Acute care surgeons (1)
- ○ Transplant surgeons (2)
- ○ Either/It depends (3)

Do transplant recipients get better care following general surgery procedures if they are cared for at transplant centers?

- ○ Yes (1)
- ○ No (2)

Should transplant recipients be transferred to transplant centers for urgent/emergent general surgery needs whenever possible?

- ○ Yes (1)
- ○ No (2)

Display This Question:

If Do you perform transplant surgery? = No

If you performed an operation on a transplant recipient, would you send them for follow up with a transplant provider?

- ○ Yes (1)
- ○ No (2)

The hospital cost ($) is higher for transplant recipients undergoing general surgery:

- ○ At transplant centers (1)
- ○ At non-transplant centers (2)
- ○ Cost is the same regardless of center type (3)

The length of stay is longer for transplant recipients undergoing general surgery:

- ○ At transplant centers (1)
- ○ At non-transplant centers (2)
- ○ Length of stay is the same regardless of center type (3)

End of Block: Reasonable Standard of Care- Txp Center ACS Surgeon

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Start of Block: Concerns

What is/would be the **most** concerning about performing general surgery on previous transplant recipients?

- ○ Wound healing complications (1)
- ○ Risk of renal failure (2)
- ○ Increased risk of mortality (3)
- ○ Management of postoperative medications (4)
- ○ Intraoperative issues (anesthesia) (5)
- ○ Anatomical differences (6)
- ○ Higher risk of other complications (7)
- ○ Other (8) _____

What is the **most important** cause of increased complications for transplant recipients following general surgery?

- ○ Steroid use (1)
- ○ Other transplant medication use (2)
- ○ History of organ failure causes irreparable damage to tissues (3)
- ○ Transplanted organs less resilient to insult (acute renal failure, acute liver failure) (4)
- ○ Other (5) _____

Display This Question:

If Do you perform transplant surgery? = No

Do you feel that your hospital is equipped to care for postoperative complications (ICU support) for transplant patients undergoing general surgery?

- ○ Yes (1)
- ○ No (2)

Display This Question:

If Do you perform transplant surgery? = No

And Is your hospital a transplant center? = Yes

The #1 reason why I would PREOPERATIVELY transfer a transplant patient needing acute care surgery to the transplant team is:

_____

Display This Question:

If Do you perform transplant surgery? = No

And Is your hospital a transplant center? = No

The #1 reason why I would PREOPERATIVELY transfer a transplant patient needing acute care surgery to a transplant center is:

_____

On a scale of 1-5, please rate what you feel to be the appropriate treatment for a transplant recipient who presents with an **urgent/emergent** general surgery need at a **non-transplant center**.

	(1) Definitely treat at non-transplant center (1)	(2) (2)	(3) Transfer if possible to a transplant center, but not necessary (3)	(4) (4)	(5) Definitely transfer to a transplant center (5)
Received transplant in past 1 year (1)	○	○	○	○	○
Received transplant in last 5 years (2)	○	○	○	○	○
Received transplant more than 5 years ago (3)	○	○	○	○	○
Transplant recipient in acute renal failure on presentation (4)	○	○	○	○	○
Transplant recipient in acute liver failure on presentation (5)	○	○	○	○	○

End of Block: Concerns

Appendix B. International Classification of Diseases, 9th Revision codes for diagnosis, procedure, inclusion and exclusion criteria for appendectomy.

Diagnosis

Appendicitis 540.0, 540.1, 540.9, 541, 542, 789.03

Procedure

Appendectomy, laparoscopic 47.07

Appendectomy, open 47.0

Inclusion

Kidney transplant recipient: V42.0

Exclusion

Other (non-kidney) transplant recipients: V42.1, V42.2, V42.6, V42.7, V42.8, V42.81, V42.82, V42.83, V42.84, V42.89, V42.9

Complications from history of other (non-kidney) transplant: 996.80, 996.82, 996.83, 996.84, 996.85, 996.86, 996.87, 996.88, 996.89

Appendix C. International Classification of Diseases, 9th Revision codes for procedure, inclusion and exclusion criteria for cholecystectomy.

Procedure

Open cholecystectomy 51.21, 51.22
Laparoscopic cholecystectomy 51.23, 51.24

Inclusion

Kidney transplant recipient: V42.0

Exclusion

Other (non-kidney) transplant recipients: V42.1, V42.2, V42.6, V42.7, V42.8, V42.81, V42.82, V42.83, V42.84, V42.89, V42.9
Complications from history of other (non-kidney) transplant: 996.80, 996.82, 996.83, 996.84, 996.85, 996.86, 996.87, 996.88, 996.89

Appendix D. International Classification of Diseases, 9th Revision codes for procedure, inclusion and exclusion criteria for colorectal resection.

Procedure

Open and other partial excision of large intestine 45.7
Open and other multiple segmental resection of large intestine 45.71
Open and other cecectomy 45.72
Open and other right hemicolectomy 45.73
Open and other resection of transverse colon 45.74
Open and other left hemicolectomy 45.75
Open and other sigmoidectomy 45.76
Open and unspecified partial excision of large intestine 45.79
Total intra-abdominal colectomy 45.8
Colostomy 46.1
Other enterostomy 46.3
Revision of large intestinal stoma 46.5
Closure of large intestinal stoma 46.6
Other repair of large intestine 46.7
Dilation and manipulation of large intestine 46.8
Other operations on large intestines 46.9
Myotomy of sigmoid colon 46.91
Myotomy of other parts of colon 46.92
Revision of anastomosis of large intestine 46.94
Pull through resection of rectum 48.4
Abdominoperineal resection of rectum 48.5

Inclusion

Kidney transplant recipient: V42.0

Exclusion

Other (non-kidney) transplant recipients: V42.1, V42.2, V42.6, V42.7, V42.8, V42.81, V42.82, V42.83, V42.84, V42.89, V42.9

Complications from history of other (non-kidney) transplant: 996.80, 996.82, 996.83, 996.84, 996.85, 996.86, 996.87, 996.88, 996.89

Appendix E. International Classification of Diseases, 9th Revision, clinical modification codes for postoperative in-hospital complications. *Adapted from Guller et al.*[26]

Mechanical Wound Delayed wound healing, 998.83 Postoperative hematoma, 998.12 Postoperative seroma (non-infected), 998.13 Disruption of operative wound, 998.3 Persistent postoperative fistula, 998.6
Infectious Postoperative infection, 998.5 Postoperative skin abscess, 998.59 Postoperative septic wound complications, 998.59 Postoperative skin infection, 998.59 Postoperative intraabdominal abscess, 998.59 Postoperative subdiaphragmatic abscess, 998.59 Postoperative infected seroma, 998.51
Urinary Postoperative urinary retention, 997.5 Postoperative urinary tract infection, 997.5
Pulmonary Postoperative atelectasis, 997.3 Postoperative pneumonia, 997.3 Postoperative acute respiratory insufficiency, 518.5 Postoperative acute pneumothorax, 512.1 Adult respiratory distress syndrome, 518.5 Postoperative pulmonary edema, 518.4
Gastrointestinal tract Postoperative small-bowel obstruction, 997.4 Postoperative ileus, 997.4 Postoperative ileus requiring nasogastric tube, 997.4 Postoperative nausea, 997.4 Postoperative vomiting, 997.4 Postoperative pancreatitis, 997.4 Complication of anastomosis of gastrointestinal tract, 997.4
Cardiovascular Postoperative deep venous thrombosis, 997.79 Postoperative pulmonary embolism, 415.11 Postoperative stroke, 997.02 Phlebitis or thrombophlebitis from procedure, 997.2 Cardiac arrest/insufficiency during or resulting from a procedure, 997.1
Intraoperative Accidental puncture or laceration, complicating surgery, 998.2 Foreign body accidentally left during procedure, 998.4 Hemorrhage/bleeding complicating procedure, 998.11

Curriculum Vitae

_____ March 21, 2017

Sandra Renae DiBrito, MD

DEMOGRAPHIC AND PERSONAL INFORMATION

Current Appointments

2012-present Halsted General Surgery Resident, Johns Hopkins University
2015-present Research Fellow, Johns Hopkins Bloomberg School of Public Health

Personal Data

Address Johns Hopkins Hospital, Department of Surgery
600 N. Wolfe St, Tower 110, Baltimore MD 21287
Tel 970-409-8005
E-mail dibrito@jhmi.edu

Education and Training

2008	BS, Molecular Biology, minors in Chemistry, Mathematics, and Physics; *summa cum laude*, University of Denver/ Denver CO
2012	MD, Medicine, Boston University School of Medicine / Boston MA
2018	PhD candidate, Clinical Investigations, Johns Hopkins Bloomberg School of Public Health / Baltimore MD (primary mentors: Dorry Segev, MD PhD; Jacqueline Garonzik-Wang, MD PhD)
2020	General surgery residency, Johns Hopkins University / Baltimore MD

Professional Experience

09/2004 – 08/2005	Research Assistant, University of Denver Department of Biology / Denver CO
09/2004 – 08/2006	Greenhouse Manager, University of Denver Department of Biology / Denver CO
06/2006 – 12/2007	Research Assistant, Eleanor Roosevelt Institute / Denver CO
09/2007 – 08/2008	Tutor in Math, Chemistry, Biology, A+ Personal Tutoring / Denver CO
09/2007 – 08/2008	Instructor, Kaplan MCAT Preparatory Program / Denver CO
06/2009 – 08/2009	Extern in Reproductive Health, Family Care Medical Center / Denver CO
07/2015 – present	Course Instructor, Medical Student Surgery Clerkship, Johns Hopkins University / Baltimore MD

PUBLICATIONS:

Original Research [** denotes co-first authorship. Role in multi-authored articles is indicated as follows if not first or last author: C = concept design, D = data acquisition, A = analysis, W = drafting/writing, R = revision]*

1. McAdams-DeMarco MA, King EA, Luo X, Haugen C, **DiBrito S**, Schaffer A, Kucirka LM, Desai NM, Dagher NN, Lonze BE, Montgomery RA, Walston J, Segev DL. Frailty, Length of Stay, and Mortality in Kidney Transplant Recipients: A National Registry and Prospective Cohort Study. *Annals of Surgery*. 12.2017; 266(6):1084-1090 *[WR]*
2. Hicks CW, **DiBrito SR**, Magruder JT, Weaver ME, Barenski CM, Heller J. Radiofrequency Ablation with Concomitant Stab Phlebectomy Increases Risk of Endothermal Heat Induced

Thrombosis: A Propensity-Matched Analysis. *Journal of Vascular Surgery*. 03.2017; 5(2):200-209 *[DAWR]*

3. Hicks CW, Liu J, Yang W, **DiBrito S**, Johnson DJ, Brito A, Higgins R, Frank SM, Wick E. A Resident-based choosing wisely quality improvement initiative to reduce unnecessary transfusions in an academic department of surgery. *American Journal of Surgery*. 10/2017. 214(4):571-576.*[CWR, SI/QI]*
4. Alejo J, Luo X, Massie AB, Henderson M, **DiBrito S**, Locke JE, Purnell T, Boyarsky B, Anjum S, Halpern S, Segev DL. Patterns of primary care utilization before and after living kidney donation. *Clinical Transplantation*. 07/2017; 31(7). *[AWR]*
5. Chow EK, **DiBrito S**, Luo X, Wickliffe C, Massie AB, Locke JE, Gentry SE, Garonzik-Wang J, Segev DL. Long cold ischemia times in same hospital deceased donor transplants. *Transplantation*. 09/2017. *Epub ahead of print [CAWR]*
6. **DiBrito SR***, Henderson ML*, Thomas AG, Holscher CM, Shaffer AA, Bowring MG, Purnell TS, Massie AB, Garonzik-Wang J, Waldram M, Lentine KL, Segev DL. Living Multi-organ Donors in the United States. *Transplantation*. 01.2018; *Epub ahead of print*.
7. **DiBrito SR**, Cerullo M, Goldstein S, Ziegfeld S, Stewart FD, Nasr I. Reliability of Glasgow Coma Score in Pediatric Trauma Patients. *Journal of Pediatric Surgery*. 01/2018. (*In press*)
8. Van Pilsum Rasmussen S, Konel J, Warsame F, Ying H, Buta B, Haugen C, King E, **DiBrito S,** Varadhan R, Rodríguez-Mañas L, Walston J, Segev D, McAdams-DeMarco M. Engaging Clinicians and Patients to Assess and Improve Frailty Measurement in Adults with End Stage Renal Disease. *BMC Nephrology*. 01.2018. 19(1):8. *[CDWR]*
9. **DiBrito SR**, Henderson ML. Should trauma surgeons treat a severely injured patient for the sake of elucidating preferences about organ donation? *AMA Journal of Ethics*. 2018. *(in press)*.
10. **DiBrito SR**, Jones C. What are the ethical implications of regionalization of trauma care? *AMA Journal of Ethics*. 2018. *(in press)*.
11. Holscher CM, Jackson K, Chow EK, Thomas AG, Haugen CE, **DiBrito SR**, Purcell C, Ronin M, Waterman AD, Garonzik-Wang J, Massie AB, Gentry SE, Segev DL. Kidney exchange match rates in a large multicenter clearinghouse. *American Journal of Transplantation*. 2018. *(in press)*
12. Jan S, Ragunanthan B, **DiBrito SR**, Omolabake A, Gutierrez MJ. Cefepime Efficacy and Safety in Children: A Systematic Review and Meta-Analysis. *Frontiers in Pediatrics - Pediatric Infectious Diseases*. 2018 *(in press) [CDAWR]*
13. **DiBrito SR**, Olorundare IO, Holscher CM, Landazabal C, Orandi BJ, Dagher NN, Segev DL, Garonzik-Wang J. Surgical Approach, Cost, And Complications of Appendectomy in Kidney Transplant Recipients. *Clinical Transplantation*. 2018. *(in press)*

Case Reports

1. **DiBrito SR**, Stephens RS. Unpredictable Location of Central Line. *JAMA Surg*. 2014 Aug; 149(8): 871-872.
2. Ladd MR, Shaw K, Munoz-Blanco S, Gilmore M, **DiBrito SR**, Eloundou SN, Stevens K, Nasr IW, Stewart FD. A Case of a Gunshot Wound to the Fetus in Utero. *Journal of Trauma and Acute Care Surgery*. 2017 Apr; 82(4):814-816.

Book Chapters, Monographs

1. **DiBrito SR** and Duncan MD. (2016). Management of Small Bowel Obstruction. Cameron JL, Cameron AM (Eds): Current Surgical Therapy, 12e (Current Therapy). Philadelphia, PA: Elsevier Saunders.
2. Blair AB, **DiBrito SR**, Duncan MD. (2018). Malignant Diseases of the Gallbladder and Bile Ducts. Rosenthal RA, Katlic MR, Zenilman ME (Eds): Principles and Practice of Geriatric Surgery, 3e New York, NY: Springer. 1-17. doi:10.1007/978-3-319-20317-1_71-1

3. **DiBrito SR** and Haut E. (2018). Interactions with Residents. Yoon-Flannery K, Fisher CS, Neff MA (Eds): A Surgeon's Path: Navigating Your Career After a General Surgery Residency. New York, NY: Springer. *In press*

Editorials

1. **DiBrito SR**, Makary M. Forecasting Hospital Readmission After Surgery: Data and the Hard-to-Measure Role of Culture. *JAMA Surg.* 2014 May; 149(5): 445-446.
2. **DiBrito SR**, Holscher CM, Haugen CE, Leeds I, Jackson K, Overton H, King E, Haut E. The Modern Surgeon Scientist. *Annals of Surgery.* 2017. *(In press).*
3. Leeds I, **DiBrito SR**, Sacks B. How we measure surgical trainee performance matters. *JAMA Surgery.* 2017. *(In press).*

FUNDING

EXTRAMURAL Funding

Current:

07/2015 – 06/2018
"Health Care Utilization and Race: Live Kidney Donor Risks and Outcomes"
Ruth L Kirschstein National Research Service Award, F32
#F32DK105600
NIDDK, NIH
$221,970
Principal Investigator, 95% effort

08/2017 – 08/2018
"Using Financial Incentives to Increase Live Kidney Donor Follow-up Compliance"
Living Legacy Foundation Grant
$10,000
Co-investigator, grant writer, 5% effort
Jacqueline Garonzik-Wang MD PhD, PI
Johns Hopkins University School of Medicine, Epidemiology Research Group in Organ Transplantation

Previous:

11/2005 –12/2005
Marsico Student Research Grant
Marsico Research Initiative
$2,500
Co-investigator, grant writer
Dennis Barrett PhD, PI
Research Scholar at University of California, Bodega Bay Marine Laboratory 100% effort

INTRAMURAL Funding

Previous:

11/2006 – 12/2006
Partners in Scholarship, Student Travel Grant
University of Denver
$1,500
Research Scholar at Oklahoma Medical Research Foundation

Education Intramural Funding

04/2017
Residents as Teachers and Leaders, Travel Grant
Johns Hopkins Hospital, Department of Surgery
$1,000
Funding to travel to and attend American College of Surgeons sponsored course

SYSTEM INNOVATION AND QUALITY IMPROVEMENT ACTIVITIES

System Innovation and Quality Improvement efforts within JHMI:

06/2016 Team organizer QI project/1% effort; Johns Hopkins Department of Surgery, Recognizing Surgical Team Members, inpatient surgical units, results: trending patient satisfaction with recognizing providers on their surgical teams following distribution of "face sheets" indicating team members and their roles.

System Innovation and Quality Improvement Program Building/Leadership:

01/2016 – 07/2017 General Surgery Representative/1% effort; House Staff Patient Safety and Quality Council, 2016 project: Sepsis Bundle Compliance, 1 hour monthly meeting and outside activities

10/2016 Institutional Representative, Residents Leading Quality Course at American College of Surgeons National Meeting, 8 hour course on performing quality improvement projects

ORGANIZATIONAL ACTIVITIES

Journal peer review activities

1/2017 Trauma Surgery & Acute Care Open, junior reviewer under Elliott Haut MD PhD

Administrative Appointments

2012 - 2018 Representative, General Surgery Residency Review Committee, Johns Hopkins Hospital
2013 - 2015 Director, Zayed Workroom Improvement Workgroup, Johns Hopkins Hospital
2013 - 2017 Leader, Surgery Department Spirit Campaign, Johns Hopkins Hospital
2013 - present Interviewer, General Surgery Residency Admissions Committee, Johns Hopkins Hospital
2016 Member, Sentinel Event Root Cause Analysis Team (retained foreign body), Johns Hopkins Hospital
2017 Member, Joy in Medicine Working Group on Clinical and Academic Success, Johns Hopkins Hospital
2018 Member, Multicenter Trials Committee, Eastern Association for the Surgery of Trauma

Professional Societies

08/2012 – present American College of Surgeons, resident member
09/2015 – present Association of Academic Surgeons, resident member
09/2015 – present American Society of Transplant Surgeons, resident member
03/2016 – present Association of Women Surgeons, resident member
05/2016 – present Pediatric Trauma Society, member
01/2017 – present Eastern Association for the Surgery of Trauma, provisional member

Conference Organizer

5/14/2016 "Spotlight on Gastric Cancer", No Stomach for Cancer National Meeting, Johns Hopkins Hospital, Local team leader

RECOGNITION

Awards, Honors

2004 – 2007 Chancellor's Scholarship
2004 – 2007 Leda B. Schwartz Scholar, Biological Sciences

2004 – 2007	University of Denver Honors Program
2006, 2007	Stczyen Premedical Scholarship
2007	Phi Beta Kappa (inducted as a junior, selected as induction speaker)
2011	Gold Humanism Honor Society
2016, 2017	Poster of Distinction, Academic Transplant Congress
2016	Distinguished Teaching Society of Johns Hopkins School of Medicine
2017	Mark M. Ravitch Award for Scientific Writing, Dept of Surgery, Johns Hopkins Hospital
2017	Top Paper Award, Association of Women Surgeons & American Journal of Surgery

Invited Talks

JHMI/Regional

09/28/2016, 09/25/2017 "Things We Put In People: A Primer on Lines and Tubes", Johns Hopkins Department of Pediatrics, noon conference, 1 hour lecture to pediatric residents, attendings, and medical students discussing types of venous lines and various tubes to increase familiarity and improve interactions with pediatric surgery consult team

National

08/04/2017 "Near Peer Panel", KUH Summer Undergraduate Research Conference, NIH, Bethesda MD; panelist for 1 hour 30min session on pursuing careers in research, attended by appx 100 students and NIH faculty.

08/04/2017 Moderator for poster session at KUH Summer Undergraduate Research Conference, NIH, Bethesda MD

OTHER PROFESSIONAL ACCOMPLISHMENTS

Oral/Podium Presentations

1. **DiBrito SR.** Barrett D. Environmental and genetic control of cell organization and locomotion in early developmental stages of sea urchin. 2006 Marsico Research Initiative Symposium, University of Denver, Denver CO, 02/2006.
2. **DiBrito SR**, Olorundare IO, Landazabal CS, Segev DL, Dagher NN. Outcomes following appendectomy in kidney transplant recipients. 2016 Academic Surgical Congress, Jacksonville FL, 02/2016.
3. **DiBrito SR**, Olorundare IO, Landazabal CS, Segev DL, Dagher NN. Outcomes following inguinal hernia repair in kidney transplant recipients. 2016 American Transplant Congress, Boston MA, 06/2016.
4. Hicks CW, Magruder JT, Weaver ML, **DiBrito SR**, Barenski C, Heller JA. Radiofrequency ablation with concomitant stab phlebectomy increases risk of endothermal heat induced thrombosis: a propensity matched analysis. 2016 Vascular Annual Meeting, Washington DC 06/2016.
5. **DiBrito SR**, Cerullo M, Goldstein S, Ziegfeld S, Stewart FD, Nasr I. Discrepancy between on-scene and ED GCS in pediatric trauma patients. 2016 American College of Surgeons/Maryland Committee on Trauma Resident Paper Competition, Baltimore MD, 11/2016.
6. **DiBrito SR**, Cerullo M, Goldstein S, Ziegfeld S, Stewart FD, Nasr I. How reliable is GCS in Pediatric Trauma? 2016 Pediatric Trauma Society National Meeting, Nashville TN, 11/2016.
7. Cerullo M, **DiBrito SR**, Goldstein S, Ziegfeld S, Stewart FD, Nasr I. How does implementing strict triage criteria for helicopter transport affect outcomes? 2016 Pediatric Trauma Society National Meeting, Nashville TN, 11/2016.

8. Cerullo M, **DiBrito SR**, Goldstein S, Ziegfeld S, Stewart FD, Nasr I. Drivers of the geographic distribution of pediatric burns. 2016 Pediatric Trauma Society National Meeting, Nashville TN, 11/2016.
9. **DiBrito SR**, Holscher CM, Olorundare IO, Haugen CH, Alimi Y, Segev DL, Garonzik-Wang J. Outcomes following cholecystectomy in kidney transplant recipients. 2017 Academic Surgical Congress, Las Vegas NV, 02/2017.
10. Hicks CW, Liu J, Yang W, **DiBrito SR**, Johnson DJ, Brito A, Higgins R, Frank SM, Wick E. A Resident-based choosing wisely quality improvement initiative to reduce unnecessary transfusions in an academic department of surgery. 2017 Association of Women Surgeons Paper Competition, San Diego CA, 10/2017 (**presenter**).
11. Leeds IL, **DiBrito SR**, Jones C, Haut E. Assessing learning during morbidity and mortality conference with a real-time audience response system. 2017 American College of Surgeons, San Diego CA 10/2017.
12. **DiBrito SR**, Bowring MG, Rasmussen S, Haugen CE, Holscher CM, Zonnenberg N, Henderson M, Segev DL, Garonzik-Wang J. Performing General Surgery on Transplant Recipients: A Pilot Survey on Surgeon Perspectives. 2017 American College of Surgeons/Maryland Committee on Trauma Resident Paper Competition, Baltimore MD, 11/2017.
13. **DiBrito SR***, Craig-Schapiro R*, Overton H, Taylor J, Fransman R, Haut E, Sacks B. Meet your Surgical Team: The Impact of a Facesheet on Patient Satisfaction. 2018 Academic Surgical Congress, Jacksonville FL 01/2018*[SI/QI]*

Posters

1. **DiBrito SR,** Hochgeschwender U. a-MSH expression in corticotrophs of the anterior pituitary. 2007 University of Denver Undergraduate Research Symposium, Denver CO 05/2007.
2. Cheng A, Carnegie D, **DiBrito SR,** Choti MA. Sterile manipulation image viewer in the Operating Room. 2013 Johns Hopkins Imaging Conference, Baltimore MD, 11/2013. (**presenter**)
3. Bae S, Durand C, Kucirka L, **DiBrito SR**, Avery R, Garonzik-Wang J, Segev DL. Early Steroid Withdrawal and Infection in Kidney Transplant Recipients. 2016 American Society of Transplant Surgeons Winter Meeting, Miami FL, 02/2016; 2017 American Transplant Congress, Chicago IL, 04/2017.
4. **DiBrito SR**, King EA, O'hare M, Segev DL. Socioeconomic status and readmission following kidney transplant. 2016 American Society of Transplant Surgeons Winter Meeting, Miami FL, 02/2016
5. Dagher NN, **DiBrito SR**, Olorundare IO, Landazabal CS, Segev DL. Outcomes following appendectomy in liver transplant recipients. 2016 American Transplant Congress, Boston MA, 06/2016. (**presenter**)
6. Dagher NN, **DiBrito SR**, Olorundare IO, Landazabal CS, Segev DL. Outcomes following inguinal hernia repair in liver transplant recipients. 2016 American Transplant Congress, Boston MA, 06/2016. (**presenter**)
7. **DiBrito SR**, Olorundare IO, Landazabal CS, Segev DL, Dagher NN. Outcomes following inguinal hernia repair in patients with end stage liver disease. 2016 American Transplant Congress, Boston MA, 06/2016.
8. **DiBrito SR**, Holscher CM, Olorundare IO, Haugen CH, Alimi Y, Segev DL, Garonzik-Wang J. Outcomes following cholecystectomy in kidney transplant recipients. 2017 American Society of Transplant Surgeons Winter Meeting, Miami FL, 01/2016.
9. **DiBrito SR**, Holscher CM, Olorundare IO, Haugen CH, Alimi Y, Segev DL, Garonzik-Wang J. Outcomes following cholecystectomy in kidney transplant recipients. 2017 American Society of Transplant Surgeons Winter Meeting, Miami FL, 01/2016.

10. **DiBrito SR**, Alimi Y, Holscher CM, Olorundare IO, Garonzik-Wang J, Segev DL. The cost of colectomy after kidney transplantation. 2017 American Society of Transplant Surgeons Winter Meeting, Miami FL, 01/2016.
11. Cerullo M, Goldstein S, **DiBrito SR**, Noje C, Ziegfield S, Stewart FD, Robertson C, Jackson E, Nasr I. A predictive model for improved disposition of pediatric traumatic brain injury patients. 2017 American Pediatric Surgery Association, Hollywood FL, 05/2017.
12. Leeds I, Canner J, Gearhart S, **DiBrito SR**, Efron J, Fang S, Safar B. Extended venothromboembolism prophylaxis after colorectal cancer surgery is not justified without further risk stratification. 2017 American Society of Colon and Rectal Surgeons Annual Scientific Meeting, Seattle WA, 06/2017.
13. Rasmussen S, Konel J, Ying H, Haugen C, King E, **DiBrito S**, Segev D, McAdams-DeMarco M. Engaging Clinicians and Patients Regarding Frailty Assessment in Kidney Transplant Candidates. 2017 American Transplant Congress, Chicago IL, 04/2017.
14. Bae S, Durand C, Kucirka L, **DiBrito S**, Avery R, Garonzik-Wang J, Segev D. Trends in Infection Among Kidney Transplant Recipients, 1999-2013. 2017 American Transplant Congress, Chicago IL, 04/2017.
15. Holscher CM, Henderson ML, **DiBrito SR**, Thomas AG, Shaffer AA, Bowring MG, Purnell TS, Massie AB, Garonzik Wang J, Waldram M, Lentine KL, Segev DL. Living Multi-organ Donors in the United States: What Do We Know? 2017American College of Surgeons Clinical Congress, San Diego CA. 10/2017.
16. **DiBrito SR**, Bowring MG, Rasmussen S, Haugen CE, Holscher CM, Zonnenberg N, Henderson M, Segev DL, Garonzik-Wang J. Who Should Operate on Transplant Recipients? 2018 American Society of Transplant Surgeons Winter Meeting, Miami FL. 01/2018.

Community Services

2004-2005	Volunteer, Denver Botanical Gardens, 1hr per week / Denver CO
2006-2007	Volunteer, St. Anthony's Hospital, Department of OBGYN, 3hrs per week / Denver CO
2006 - 2012	Producer, director, cast member of The Vagina Monologues at University of Denver, Boston University School of Medicine; raised over $25,000 for women's charities
10/18/2016	Volunteer, Medical Student Mock Interviews, American College of Surgeons, 2 hours / Washington DC
2016-present	Maryland Responds Medical Reserve Corps / Baltimore MD

Biosketch

Dr. Sandra R. DiBrito was born on June 29, 1986 in Pueblo, Colorado, and raised in Silverthorne, Colorado. She was the valedictorian of Summit High School, Class of 2004. She attended the University of Denver on a Chancellor's scholarship, where she participated in the University Honors program. She conducted basic science research at the Eleanor Roosevelt Institute under the guidance of Dr. Miles Brennan and wrote her undergraduate thesis on the pro-opiomelanocortin gene and its products in a mouse model. She graduated *summa cum laude* in 2007 with a B.S. in Molecular Biology and minors in Chemistry, Mathematics, and Physics. She pursued medical school at Boston University School of Medicine, and outside of her coursework, produced and directed four annual performances of The Vagina Monologues, raising over $25,000 for women's charities in Boston. In 2012, she began her General Surgery residency at The Johns Hopkins Hospital. After receiving a National Institute of Health Ruth L. Kirschstein F32 National Research Service Award, she joined the Epidemiology Research Group in Organ Transplantation, led by Dr. Dorry Segev, to pursue her PhD in Clinical Investigations at the Johns Hopkins Bloomberg School of Public Health. Dr. DiBrito was inducted into the inaugural class of the Distinguished Teaching Society of the Johns Hopkins School of Medicine in 2016, and during her time in the research lab, she participated weekly in medical student education as a Halsted Teaching Resident. After completing her clinical training, she plans to pursue a fellowship in trauma and acute care surgery. In her free time, Dr. DiBrito enjoys being outdoors, traveling, and spending time with her two sons, Maxwell and Franklin, her wife, Kate, and her dog, Violet.